The long-term respiratory health effects of the herbicide, paraquat, among Western Cape workers

Mohamed Aqiel Dalvie

The long-term respiratory health effects of the herbicide, paraquat, among Western Cape farm workers

Mohamed Aqiel Dalvie
BSc (Physiology, Chemistry); BSc Med Hons (Sportscience)

This thesis is presented in fulfilment of the requirements for the degree of Masters in Community Health (Msc) in the Department of Community Health, Faculty of Medicine, University of Cape Town, 1996. The work on which this thesis is based is original research and has not, in whole or in part, been submitted towards another degree, at this University or elsewhere. The University is empowered to reproduce either the whole or any portion of the contents for purposes of research.

August 1996

ABSTRACT

Objective: Paraquat is a commonly used herbicide worldwide and is a well documented cause of pulmonary fibrosis in studies of laboratory animals and in humans following high dose exposure (usually accidental or as parasuicide). The respiratory effects of long-term, low dose paraquat exposure have not been fully evaluated. We set out to evaluate the possible effects of paraquat spraying among deciduous fruit farm workers in the Western Cape, South Africa.

Methods: A cross-sectional study of 126 workers was performed. Administered questionnaires generated information on exposure, respiratory symptoms and confounding variables. Spirometry and gas transfer were measured and chest radiographs performed. Oxygen desaturation on exercise testing was by oximetry during a modified stage one exercise test.

Results: No association was found between long-term paraquat exposure and reported symptoms, spirometry (FVC, FEV1, FEV1/FVC) and gas transfer(T_{Lco} and K_{co}) or chest radiography. Multivariate analysis showed a significant relationship between measures of long-term paraquat exposure and arterial oxygen desaturation during exercise ($p < 0.05$).

Conclusion: Previous studies have also not shown a significant relationship between measures of paraquat exposure and standard

tests of lung function. Arterial oxygen desaturation during exercise represents a more sensitive test. Our findings indicate that working with paraquat under usual field conditions for a long period is associated with abnormal exercise physiology in a dose dependant fashion.

ACKNOWLEDGEMENTS

I wish to thank The International Research and Development Centre (IDRC), Medical Research Council of South Africa and the Guy Elliot Fellowship in the Department of Medicine UCT for their financial support for the project.

To Marcus Medical for lending the lung function apparatus and providing technical staff for the setting up of the equipment.

To Ceres Hospital for providing the space and involving personnel during data collection.

To Dr Neil White for his important contributions in the planning and execution of the project and for his constructive comments and sound advice during co-supervision of the thesis.

To Professor Johnny Myers for his invaluable guidance, insights and advice during the execution of the project and co-supervision of the thesis.

To Dr Ricky Rain for his supervision of and advice on the clinical respiratory health measurements in the study.

To Professor Dave Christiani for his worthwhile comments on the project.

To the farmers and farm workers of the Kouebokkeveld for

participating in the project.

To all the staff of the research project including interviewers, technologists and technicians for working hard and efficiently during data collection. In particular, Aneleh Midgely, for her competent administration and quality control of the data. And to Hanlie van Heerden and Mandy Vorster for their difficult roles as liaison person and lung function technologist, respectively. Also to Eddie Langeveld and his wife, Pat for their hospitality and assistance with the interviewers.

To Dr Leslie London for his inestimable assistance during the project which stemmed from his investigation of organo-phosphate pesticides.

To Mary Lou Thompson for her advice on statistical analysis.

To the staff of the Department of Community Health for providing a pleasant working environment. In particular, Dot Manly who was always willing to be of assistance.

SUMMARY OF CONTENTS

CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

CHAPTER 1 A REVIEW OF PARAQUAT AND AN OUTLINE OF THE OBJECTIVES OF THIS STUDY

1.1 Introduction

Pesticides can simply be described as substances used to combat unwanted living organisms (pests), although there are more formal definitions given by institutions such as the FAO, the Codex Alimentarius Commission (Codex) and the Council of Europe. Pesticides are used in vector control programmes, horticulture, forestry and livestock production and refer mostly to chemicals that are used in agriculture for the control of pests, weeds, or plant diseases (agro-chemicals). These include insecticides, herbicides, fungicides, fumigants and molluscicides.

The industrial production of pesticides has increased substantially since the Second World War and in 1985 over 3 million tones of formulated pesticides were produced globally (1). Awareness of the environmental and public health impacts of pesticides has increased since the 1960's when the dangers of DDT and other organochlorine pesticides became apparent and more legislative controls were introduced in first world countries. Pesticide use is presently still increasing, particularly in Third World countries. New pesticides are continually being formulated to increase agricultural productivity.

Agriculture is one of the biggest sources of employment in South

Africa. The use of pesticides in this country has increased at a similar rate as that of developing countries, as reflected by total expenditure on pesticides in 1978-79 (2) and 1990 (4). Over 24 000 tons of pesticides were sold in South Africa in 1978-79.

The Western Cape is an important agricultural region in South Africa (market research shows that more than 7000 tons of pesticides were sold in the Southern region of South Africa in 1989, 4). More than 150 000 workers were employed in this region in 1991 (5). Although maize farming is the largest agricultural activity in South Africa, deciduous fruit farming is most important in the Western Cape where the nature of agricultural production differs from the rest of the country.

Working and living conditions of farm workers and rural populations, are generally poor (6).

1.2 Paraquat

Paraquat was introduced commercially in 1961 and is globally one of the two most widely used herbicides (used in more than 130 countries) (7). Its use is banned in Finland, Sweden and Austria, restricted in Hungary and the United States and cancelled in Norway; it has limited registration in Germany and The European Council is currently reviewing paraquat for registration (7).

Paraquat has been one of the most commonly used herbicides in South Africa for the last twenty two years. It is used in all forms of fruit farming (8).

Available information on herbicide and paraquat usage patterns in South Africa are summarised in table 1.1

1.2.1 Physical and chemical properties of paraquat

Paraquat is a bypyridylium compound (1,1'-dimethyl-4,4'bipyridylium dichloride or 1,1'-dimethyl-4,4-bipyridylium dimethylsulfate). In aqueous solution it is non-explosive, non-flammable, non - volatile and corrosive.

Paraquat readily undergoes a single-electron reduction to the cation radical which is important for its herbicidal activity and toxic effects.

Analytical methods for detection of paraquat in soil, water, air, biological tissues and plants include spectrophotometry, gas chromatography and radio-immuno-assay. The most sensitive measurement on biological tissues is gas chromatography with detection limits of 0.025 ug/ml (9).

Table 1.1 Summary of herbicide and paraquat usage patterns in South Africa

	SA*	Southern Region$
Herbicides :		
Weight (metric tons)	6083	713
% of total pesticides	24.7%	10%
BEU+ (10^6 x kg)	/	1001
% of total pesticides	/	2.4%
Sales (R million)	282	51
% of total pesticides	46%	29%
Paraquat:		
Weight (metric tons)	129	59
% of total herbicides	2%	8%
BEU+ (10^6 x kg)	/	390
% of total herbicides	/	39 %

* Annual pesticide use in the Republic of South Africa in 1978 - 1979 (2); Sales figures are for 1990 (8)

$ Agrochemical usage patterns in the southern region of South Africa (Western and Eastern Cape; 4, 8); based on market research data of 1990

+ BEU: biological equivalent units (method used for weighting usage by relative toxicity)

1.2.2 Classification of toxicity

South Africa uses the WHO toxicity classification, which is based on individual acute LD50's (lowest dosage that kills 50% of test animals) for pesticides. According to this classification paraquat, that has an oral LD_{50} of 150 mg/kg body weight and a dermal LD_{50} of 236 mg/kg body weight, is a group 2 toxin[1]. According to current legislation, paraquat[2] is safe under normal production conditions and has no chronic effects on sprayers.

1.2.3 Environmental effects

Unlike pesticides such as DDT, paraquat is not persistent in the environment. It is degradated by soil micro-organisms, is inactivated by becoming strongly bound to clay particles and is adsorbed on aquatic weeds. Paraquat is also not volatile following spraying.

Its low cost relative to other herbicides on the market has been an additional favourable factor governing its use.

1.2.4 Agricultural application

Paraquat is a non-selective, broad spectrum, contact herbicide and is also used as a desiccant or cotton defoliant(9).

---

[1] The second highest toxicity category out of 4

[2] Registered under Act 36 with no restictions

In South Africa, several formulations (granules or liquid concentrates) which include paraquat, preeglone and gramoxone are available. The paraquat content in these products, which are highly toxic and corrosive in their concentrated forms, may vary from 10% to 20 % (W/V, V/V). The final working concentration ranges between 1 to 5 grams/litre active ingredient in water (ICI - Kynoch Spray Programmes, Agrochemicals, 1991).

1.2.5 Occupational exposure and absorption

Herbicides are used in lesser quantities than other pesticides because they require fewer applications (2-3 times per year) and are expensive. They are applied to the ground in the deciduous fruit sector in the Western Cape because spraying has to be directed downwards on to weeds. Usually a tractor is used for spraying. The herbicide is dispensed by a low boom or through hand held sprayguns or rubber hoses. Spraying also occurs from a backpack through a hand-held nozzle.

Regular exposure to a highly toxic compound such as paraquat might present an occupational hazard to workers. This is particularly important in conditions where there is a lack of product knowledge and safety awareness as is the case in South Africa. Previously reported total (respiratory and skin) exposures of 12-170 mg/kg bodyweight/hour of knapsack sprayers (10) are higher than paraquat doses which cause chronic injury in animals (11-14). Long term skin exposure to paraquat may be an important route of exposure (15). Healthy human skin has been

found to have low absorption values to paraquat at working concentrations (16), but there is still uncertainty about the level of paraquat in plasma. Workplace exposures measured previously (10, 17) did not include high exposure tasks such as mixing. Long term skin contact in humans may cause blisters and ulcers, which might increase paraquat absorption (18) particularly in applicators and mixers.

1.2.6 Acute effects

Acute effects are well documented in the literature from both animal studies and case reports of accidental and suicidal paraquat poisoning. Large oral doses of paraquat (more than 10 mg/kg body weight) cause multi-organ acute injuries especially to kidneys and lungs, which are the organs with maximal tissue dose with respect to both intensity and duration. Poisoning is often fatal at high doses (9,11,18).

Lower sublethal doses of paraquat administered as a bolus (less than 10 mg/kg body weight) result mainly in chronic lung injury in laboratory animals (11-14) including effects on lung compliance and arterial oxygen levels in sheep (12), radiological and histological changes in cynomolgous monkeys, (13) and histological changes in rats (11). Acute toxicity is believed to occur when paraquat, for which lung cells have a high affinity, becomes absorbed and damages alveolar epithelial cells leading to inflammation (alveolitis) and eventually fibrosis (11). The effect on lung function seems to occur gradually over a period

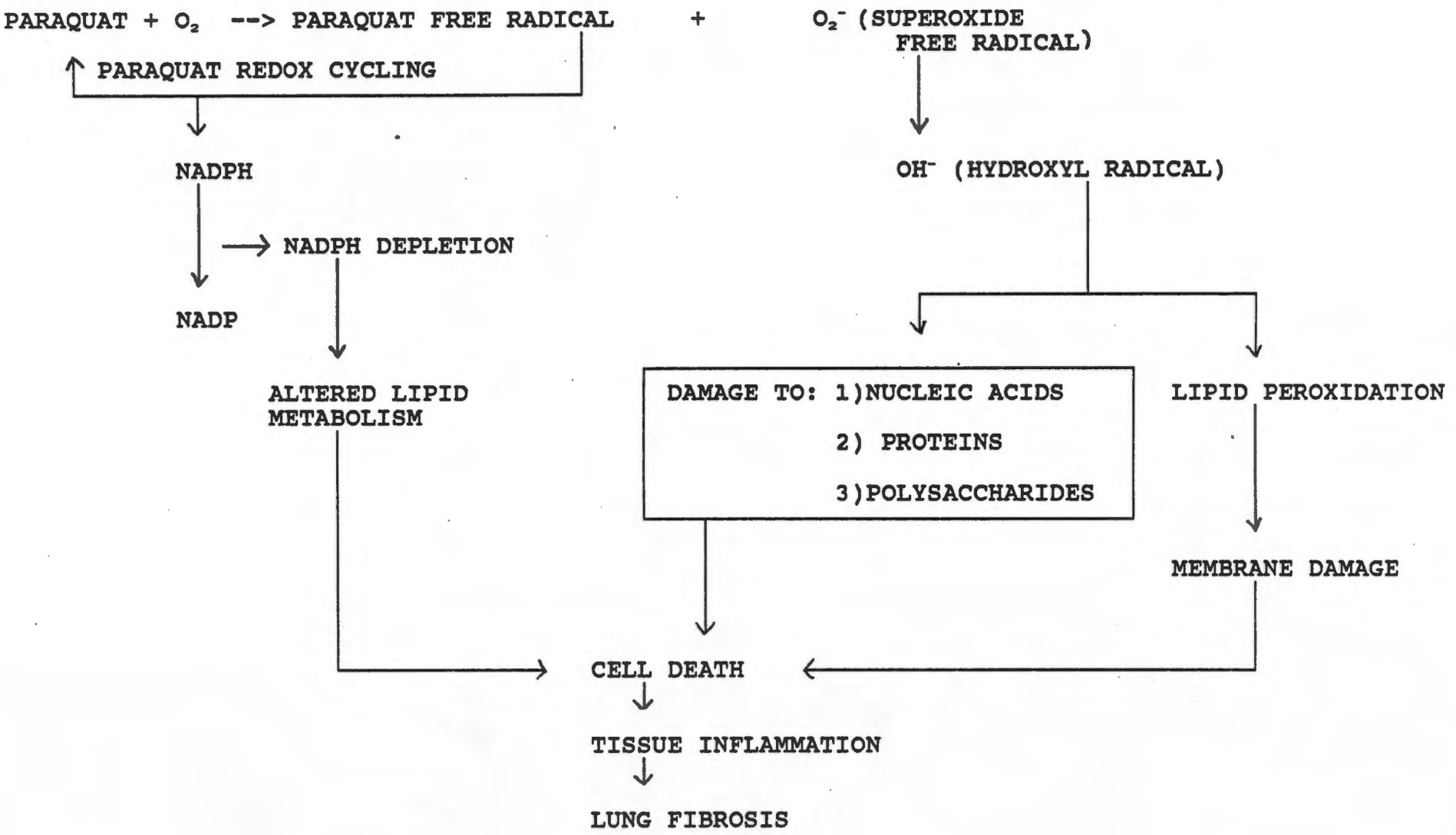
of several weeks.

The mechanism by which paraquat causes injury is most commonly believed to occur through its reaction with oxygen to form toxic oxygen radicals (9). The primary biochemical mechanism of paraquat cell toxicity is currently believed to occur by the cyclic redox reactions of paraquat with reducing equivalents and oxygen in the cell leading to the consumption of NADPH and the production of superoxides (19). There is still uncertainty about subsequent events. Either the consumption of NADPH could lead to cell death or the production of superoxides could initiate a series of events causing toxicity. Figure 1.1 Summarises the primary biochemical mechanism of paraquat cell toxicity.

Human case reports post sublethal acute poisoning effects (20-22) have indicated similar events where lung damage may occur in the form of interstitial fibrosis and medial arteriolar hypertrophy. The first detectable change reported associated with such exposures has been an asymptomatic reduction in transfer factor for carbon monoxide. Pulmonary toxicity may be progressive months after exposures has taken place. Symptoms are predominantly dyspnoea and the chest radiograph shows linear shadowing. Subsequent events appear to be related to the dose responsible for initial poisoning. Either lung damage proceeds to pulmonary fibrosis and death, or there is a gradual improvement with some residual fibrosis and/or pulmonary hypertension.

Community exposure to paraquat drift sprayed by helicopter have increased 2-wk self reported respiratory symptoms which included coughing, trouble breathing, unusual tiredness and wheezing (23).

Figure 1.1 The proposed biological mechanism of paraquat lung toxicity



1.2.7 Long term effects

The respiratory effects of long term low dose exposure to paraquat have not been studied extensively although studies have been performed on industrial and farm workers (table 1.2). Gutierrez et al. (personal communication with C. Hogstedt) investigated Nicaraguan banana plantation workers and found an effect on reported respiratory disease symptoms but on spirometry. Other studies (17,24.1, 25, 26,27) have used standard respiratory function tests including spirometry and gas transfer, and have also not found a relationship between paraquat exposure and functional or clinical abnormalities. Although standard respiratory function tests would normally be regarded as being adequate to indicate restrictive abnormalities in pulmonary fibrosis, it is still not clear whether these tests are sensitive enough to measure the abnormalities suggested by the symptoms in the Nicaraguan study.

Another factor which might explain the negative results of previous studies is insensitive exposure measurements. In most studies performed, lifetime cumulative days of exposure estimated from work history was the only method of estimating long-term paraquat exposure. The Nicaraguan study used symptoms of paraquat usage to identify a high exposure group and which was found to have a respiratory defect. No previous study incorporated job history variables other than duration in

exposure calculations. This might have resulted in non differential exposure misclassification which might have diluted or missed exposure-response relationships.

Reduced compliance and increased alveolar - arterial oxygen tension difference have, previously been documented in sheep with long term low dose parenteral exposure to paraquat and subsequent development of chronic lung disease (12).

Table 1.2 Summary of epidemiological studies which investigated the long term effects of paraquat exposure.

Authors	Study sample	Year	Methods	Assc
Swan	Malaysian rubber workers (n = 38)	1969	Radiography (trial)	none
Howard	English, Malaysian formulation workers (n = 36)	1979	Health records (incl. respiratory symptoms	none
Howard	Malaysian formulation workers (n = 24)	1981	Spirometry	none
			Transfer factor	none
Gutierrez* etal	Nicaraguan banana plantation workers (n= 136)	1988	Respiratory symptoms	+
			Spirometry	none
Senanayake etal	Sri Lankan sprayers (n= 85)	1993	Spirometry	none
			Transfer factor	none

Assc: + = positive association, none = no association

* Unpublished

In South Africa, the long-term health effects of paraquat have not been subjected to systematic epidemiological study. Over 1,2 million workers are currently employed in the agricultural sector in South Africa (28). An unknown percentage are exposed to herbicides. Farm workers work in poor safety conditions and the incidence of environmentally related respiratory disease is likely to be high in this population. Increased prevalences of respiratory disorders including symptoms and chronic obstructive pulmonary disorders (COPD) have been well documented among European and North American farm workers. There is no comparable information about South African farm workers. However, it may be anticipated that respiratory hazards including infections, tuberculosis, indoor smoke and fume exposures, and other environmental effects are more prevalent in less developed societies.

In addition to the standard respiratory function tests used in previous paraquat studies (17, 24.1, 26, 27) this study aimed to measure one aspect of respiratory reserve in the form of exercise oximetry. The latter is notionally a more sensitive test of respiratory health. A subsidiary aim was to evaluate this test, which is a modified standard clinical exercise test and involves the measurement of oxygen saturation during exercise with oximetry, as an epidemiological tool for field use.

New information on paraquat in South Africa, given that its use is banned in some countries, has important policy implications.

These considerations led to the current study whose aims and objectives are outlined below.

1.3 Aims and objectives of the current study

AIM

To investigate the respiratory health effects of long - term low dose paraquat exposure under usual application conditions among Western Cape farm workers, independently of current acute effects of exposure or sequelae of past poisoning episodes.

OBJECTIVES

1. Measurement of workers' exposure to paraquat including long-term and acute recent exposure using a job exposure matrix, as well as acute poisoning events.

2. Measurement of the respiratory health of workers by means of:

    i) chest radiograph
    ii) symptom questionnaire
    iii) brief clinical examination
    iv) spirometry
    v) gas transfer factor
    vi) exercise performance - oxygen saturation

3. Measurement of potential confounding or effect modifying variables (eg. tuberculosis , other respiratory disorders, smoking)

4. Determination of associations between exposure to paraquat and adverse respiratory outcomes mentioned adjusting, for measured confounders and/or effect modifying factors.

5. Comparison of the sensitivity of the various measurements in detecting paraquat-related effects.

6. Assessment of the field utility of exercise oximetry.

1.4 References

1. Mowbray, DL. Pesticide use in the South Pacific. Nairobi: UNEP (UNEP Regional Seas Reports and Studies, No. 89)1988

2. Fourie HO. Toxicological consequences of pesticidal use in the Republic of South Africa [PhD Thesis]. Cape Town: Department of Community Health. University of Cape Town, 1986.

3. London L. Agrochemical Hazards in the South African farming sector. South African Medical Journal 1992a; 481: 560 - 564

4. London L, Myers J. Agrochemical usage patterns and workplace exposure in the major farming sectors in the southern region of South Africa. South African Journal of Science 1995; 91: 515 - 522

5. Central Statistical Services (CSS). Statistical News Release P1101 - Agricultural Survey. Pretoria: CSS 1991.

6. London L. An investigation into the neurological and neurobehavioural effects of long-term agrochemical exposure among deciduous fruit farm workers in the Western Cape, South Africa, 1994 [MD Thesis]. Cape Town: Department of Community Health. University of Cape Town, 1995.

7. Active ingredient fact sheet; paraquat. Pesticide News 1996; 32: 20 - 21

8. London L, Myers J. General patterns of agricultural usage in the southern region of South Africa. South African Journal of Science 1995; 91: 509 - 514

9. World Health Organisation. Paraquat and Diquat. Geneva: WHO 1984; IPCS environmental health criteria 39

10. Chester G, Woolen BH. Studies of the occupational exposure of Malaysian plantation workers to paraquat. British Journal of Industrial Medicine 1982; 38: 23 -33

11. Smith P, Heath D, Kay JM. The pathogenesis and structure of paraquat - induced pulmonary fibrosis in rats. The Journal of Pathology 1974; 114(2): 57-67

12. Shinozaki S, Bobayashi T, Kubo K, Sekigushi M. Pulmonary hemodynamics and lung function during chronic paraquat poisoning in sheep. American Review of Respiratory Disease 1992; 146: 775 - 780

13. Schoenberger CI, Rennard SI, Bitterman PB, Fukuda Y, Ferrans Vj, Crystal RG. Paraquat - indused pulmonary fibrosis. American Review of Respiratory Disease 1984; 129: 168 - 173

14. Butler C. Pulmonary interstitial fibrosis from paraquat in the hamster. Archives of Pathology 1975; 99: 503 - 7

15. Smith TJ. Exposure assessment for occupational epidemiology. American Journal of Industrial Medicine 1987; 12: 249 - 268

16. Walker M, Dugard PH, Scott RC. Absorption through human and laboratory skin: in vitro comparison. Acta Pharmarceutica Suecica 1983; 20: 52 - 53.

17. Swan AAB. Exposure of spray operators to paraquat. British Journal of Industrial Medicine 1969; 26: 322 - 329

18. Bernardini P. Paraquat and diquat: toxicological aspects and occupational hazards; Archivio di Scienze del Lavoro 1986; 331(2): 117 - 123

19. Smith LL. The response of the lung to foreign compounds that produce free radicals. Annual Review of Physiology. 1986; 48: 681 - 692.

20. Rebello G, Mason JK. Pulmonary histological appearances in fatal paraquat poisoning. Histopathology 1978; 2: 53 - 66

21. Hudson M, Patel SB, Ewen SWB, Smith LL, Friend JAR. Paraquat induced pulmonary fibrosis in three survivors. Thorax

1979; 34: 150 - 160

22. Levin PJ, Klaff LJ, Rose AG, Ferguson AD. Pulmonary effects of contact exposure to paraquat: a clinical and experimental study. Thorax 1991; 46: 201 - 204

23. Ames RG, Howd RA, Doherty L. Community exposure to a paraquat drift. Archives of Environmental Health 1993; 48(1): 47 - 49.

24. Howard JK. A clinical survey of paraquat formulation workers. British Journal of Industrial Medicine 1979; 24.136: 220 - 223

25. Lings S. Pesticide lung: A pilot investigation of fruitgrowers and farmers during the spraying season. British Journal of Industrial Medicine. 1982; 39: 370 - 376

26. Howard JK, Sabapathy NN, Whitehead PA. A study of the health of Malaysian plantation workers occupationally exposed to paraquat. British Journal of Industrial Medicine. 1981; 38: 110 - 116

27. Senanayake N, Gurunathan G, Hart TB, Amerisinghe P, Babapulle M, Ellapolla SB, Udupihille M, Basanayake V. An epidemiological study of the health of Sri Lankan tea plantation workers associated with long term exposure to paraquat. British Journal of Industrial Medicine Med 1993; 50: 257 -263

28. Central Statistical Services (CSS). Agricultural survey, CSS. Statistical News Release 1990; p.1101

CHAPTER 2 MEASUREMENT OF RESPIRATORY HEALTH USING EXERCISE OXIMETRY

2.1 Significance of measuring exercise health

During exercise physiological demands are increased due to increased energy demands thus requiring the body to use its physiological reserve. The biological significance of measuring exercise health is to test the body's physiologic reserve which might be altered in diseased persons, representing the earliest disturbances in function which may not be detected at rest.

2.1.1. The exercise test

Standard clinical exercise testing is based on the procedures developed by Jones and Campbell (1), and involves exercise (usually running or cycling) against resistance while measurements are made to assess respiratory health. These measurements which include methods for assessing ventilation, cardiac status, and gas exchange vary in sophistication depending on the type of test. Four stages test series can be performed. The stage one test involves incremental exercise to exhaustion and include basic measurements (heart rate, blood pressure, electrocardiogram, ventilation, mixed expired oxygen and carbon dioxide concentrations, O_2 saturation by oximetry and post-exercise plasma lactate concentration. The stage 2-4 tests are

performed at steady state exercise based on measurements obtained in the stage one tests and include measurements of increasing complexity to obtain more precise information from the subject.

2.1.2. Exercise gas exchange in the healthy

During exercise oxygen delivery is enhanced by increased ventilation and cardiac output. The pulmonary demands during exercise revolve around the maintenance of the arterial oxygen level above 11.4 kPa to ensure adequate supply of oxygen to exercising muscles. In normal lungs, increased pulmonary ventilation and diffusion are adequate to prevent hypoxemia as evidenced by normal values for a number of indices when compared to resting values (2-5). Invasive blood gas analysis has shown that the arterial end-tidal difference in CO_2 tension (> 0 kPa) and dead-space/tidal-volume ratio (> 0.3) which indicate wasted ventilation, as well as arterial O_2 tension (> 11.4 kPa) and alveolar O_2 difference (> 5 kPa) which measure hypoxemia remain normal during exercise in healthy persons (2-5).

2.1.3. Exercise gas exchange in the diseased

Respiratory diseases results in gas exchange abnormalities such as an increase in the amount of left to right shunting, a decrease in the oxygen concentration in mixed venous blood, maldistribution of ventilation-perfusion ratio and diffusion limitations. Despite these limitations, pulmonary reserve ensure that resting PaO_2 in the diseased subject remains normal (5, 6).

Under exercise conditions, however, pulmonary reserve is not sufficient to prevent hypoxemia (5-9).

Paraquat toxicity is associated with interstitial pulmonary alveolar disease which is a disease that results in damage to the alveolar membrane causing fibrosis and a decrease in inspiratory capacity due to stiffening of the lungs. This results in a reduction in lung volume as evidenced by the reduced tidal volumes measured in patients with restrictive defects (5). At rest a tidal volume of sufficient size can be maintained or the breathing rate could be increased to maintain adequate ventilation. During exercise increase in ventilation is limited by the tidal volume. If this cannot be increased the amount of unventilated area in the lung increases resulting in a reduction in the ventilation-perfusion ratio and eventually hypoxemia. Damage to the alveolar capillary could also result in a diffusion limitation by decreasing the time for diffusion of oxygen from the alveoli into blood. At rest the transit time of a red bloodcell in the pulmonary capillary is about 0.7 seconds and is sufficient for equilibration of arterial O_2 with alveolar O_2 in both diseased and healthy persons. During exercise however the transit time of red blood cells is reduced to 0.25 seconds due to increased blood flow. This is adequate for diffusion of oxygen in healthy persons but not in diseased persons.

2.2. Oximetry

Oximetry is a method which uses absorption spectroscopy to measure arterial oxygen saturation (SaO_2) in blood.

2.2.1. Oxygen Saturation

Oxygen in blood, binds to haemoglobin to form oxyhaemoglobin. Ninety nine percent of oxygen in blood is transported by binding to haemoglobin and the oxygen content of blood can in fact be determined by the concentration of haemoglobin (approximately 15 g/100 ml), the oxygen binding capacity of haemoglobin and the oxygen saturation of haemoglobin (percentage of total blood haemoglobin bound). The binding of oxygen to haemoglobin increases in a sigmoidal fashion as more oxygen becomes bound. This means that at venous oxygen levels (5.7 kPa) the affinity of oxygen for haemoglobin is low when compared to arterial blood (> than 14.3 kPa). Factors such as a reduced pH, increased temperature, increased carbon monoxide levels and increased diphosphoglyceride levels shift the dissociation curve to the right because of a reduced affinity of haemoglobin for O_2.

2.2.2. Apparatus

The basic measuring equipment used in oximetry consists of a probe which is connected to a recording device. The probe is made up of a light source, that emits light at known red and infrared band wavelengths, and a sensor (photodetector) which is

placed across a pulsatile vascular bed (of the finger or ear).

2.2.3. Principles of operation

During oximetry the absorbance of oxygenated and reduced haemoglobin in arterial blood are measured usually at 640 (red band) and 940 nm (infrared band) respectively in order to calculate the ratio of oxygenated over total haemoglobin (oxygen saturation). Absorbance is measured continuously to detect fluctuations during the cardiac cycle. In this way background absorbances due to connective tissue, bone and venous blood which are constant during this time, are cancelled out.

2.2.4. Limitations

Since SaO_2 is related to PaO_2 by the oxyhemoglobin dissociation curve, factors that shift the curve will affect this relationship. Because of the shape of the curve, relatively large changes in PaO_2 will result in small changes in saturation in the plateau region (14.3 - 10.7 kPa), whereas bigger changes in saturation, for small changes in PaO_2 occur at lower PaO_2 levels.

Other species of haemoglobin such as carboxyhaemoglobin (haemoglobin bound to carbon monoxide) and methaemoglobin can affect absorbances (10 - 11). Previous studies have found pulse oximetry to be highly correlated to CO-oximetry (regarded as the gold standard in oximetry because it incorporates measurements

from other haemoglobin species) at 70 -100 percent saturation levels (10, 12, 13), but a poor correlation at low saturation levels (14).

Factors such as dyes, low perfusion, anaemia, venous pulsations, and excessive light could also interfere with oximeter accuracy (10). Skin pigmentation does not interfere with oximetry readings (15).

2.2.5. Validity of exercise oximetry to estimate respiratory health

Watters (16) has shown that changes in alveolar-arterial oxygen tension and changes in saturation measured with ear oximetry correlated better with histopathologic and histologic changes than subjective clinical assessments, spirometry, diffusion capacity and radiography in patients with pulmonary fibrosis. Sue found spirometry and diffusion capacity at rest to be insensitive predictors of abnormal gas exchange when compared to changes that occurred in arterial blood gases during exercise(7). Powers subsequently showed a high (0.82 - 0.93) correlation between invasively measured oxygen saturation and pulse oximetry, thus validating the use of oximetry for measuring respiratory health (17).

2.3 References

1. Jones NL, Campbell EJM . Clinical exercise testing. 2nd ed. Philadelphia: W.B Saunders, 1982.

2. Hansen JE, Sue DY, Wasserman K. Predicted values for clinical exercise testing. American Review of Repiratory Desease 1984; 129: Suppl: S49 - S55

3. Sue DY. Normal values in adult exercise testing. Clinic in Chest Medicine. 1984; 5: 89 - 98.

4. Jones NL, McHardy GJR, Naimark A, Campbell EJM. Physiological dead space and alveolar-arterial gas pressure differences during exercise. Clinical Science 1966;31: 19-49

5. Wasserman K, Whipp BJ. Exercise physiology in health and disease. American Review of Respiratory Disease 1985; 132; 612-8

6. Ward JC, Harper, Popovich J. Diffusion capacity predicts arterial oxygen desaturation in patients with lung disease of multiple etiologies. Chest 1986; 89: 514S.abstract.

7. Sue D Y, Oren A, Hansen JE, Wasserman K. Diffusion capacity for carbon monoxide as a predictor of gas exchange during exercise. New England Journal of Medicine 1987; 316: 1301 - 6

8. Risk C, Epler GR, Gaensler EA. Exercise alveolar-arterial oxygen pressure difference in Interstitial lung disease. Chest 1984: 85 69 - 74

9. Keogh BA, Lakatos E, Price D, Crystal GR. Importance of the lower respiratory tract in oxygen transfer. American Review of Respiratory Disease 1984; Suppl S76 - S80

10. Schnapp LM, Cohen HN. Pulse oximetry. Uses and abuses. Chest 1990; 98: 1244 - 50.

11. Taylor M.B., Whitwam J.G. The current status of pulse oximetry. Anaesthesia 1986; 41: 943-9.

12. Yelderman M, New W. Evaluation of pulse oximetry. Anesthsiology 1983; 59: 349 -52.

13. New W. Pulse oximetry. Journal of Clinical Monitoring 1985; 1: 126-31

14. Severinghaus J, Naifeh K. Accuracy of response of six pulse oximeters to profound hypoxia. Anaesthesiology 1987; 67: 551 - 58

15. Bothma PA, Joynt GM, Lipman J, Hon H, Mathala B, Scribante J, Kromberg J. Accuracy of pulse oximetry in pigmented patients. South African Medical Journal 1996; 86(5) : 594 - 596

16. Watters C, King TE, Swharz MI, Waldron JA, Stanford RE, Cherniack RM. A clinical, radiographic, and physiologic scoring system for the longitudinal assessment of patients with idiopathic pulmonary fibrosis. American Review of Repiratory Desease 1986; 133: 97 -103

17. Powers SK, Dodd S, Freeman J, Ayers GD, Samson H, Mcknight T. Accuracy of pulse oximetry to estimate HbO_2 fraction of total Hb during exercise. Journal of Applied Physiology. 67(1): 300 - 304

CHAPTER 3 METHODS

3.1 Design

A cross-sectional analytic study was performed.

3.2 Population and Sampling

Ceres is an agricultural district in the Western Cape Province, South Africa. The Koue Bokkeveld is one of the two major fruit producing regions in Ceres comprising of 118 registered farms. Deciduous fruit farming is predominant.

Sampling in the core study:

In a previous study (1) 113 farms linked to the two major co-operatives in the region were contacted and of these farms 77 participated. A random sample of non-participating farms indicated that a high percentage (39.2%) were small farms (less than 25 hectares).

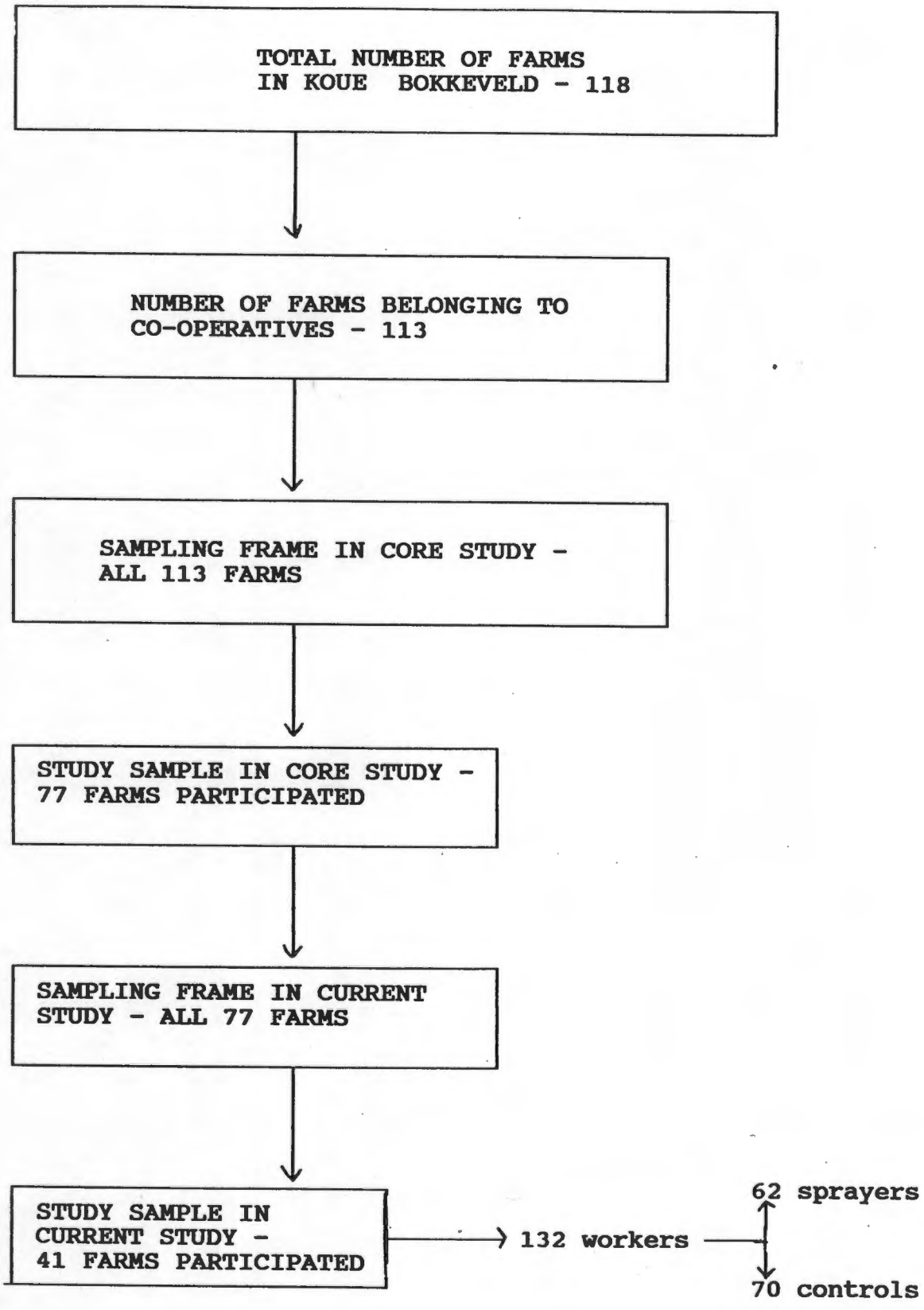
Sampling in the current study:

The 77 farms that participated in the core study were contacted. Forty-one farms agreed to participate in the current study. All current herbicide sprayers on these farms (62 sprayers) were selected. Every sprayer was matched for age, overall body size and education with one or two controls (workers not currently

spraying herbicides) from the same farm with the assistance of the farmer. A total of 132 farm workers including 70 controls were selected. Figure 3.1 outlines the manner in which the study sample was obtained.

Selection was done on current spraying status in order to achieve optimal exposure contrast in the population under study.

Figure 3.1 The manner in which the study sample was obtained.



3.2.1 Sample size calculations

Table 3.1 lists the sample sizes required in order to detect differences for respiratory symptoms, spirometry, diffusion capacity and exercise oximetry measurements at the 95% confidence level with 80% power. The differences between the exposed and control groups were obtained by estimating the smallest possible expected difference for the different outcome measures in the study. The estimated differences are subclinical (below the values regarded as clinically relevant by physicians and usually 2 standard deviations from the mean of the population). The sample size calculations indicated that the size of the study sample was sufficient to detect significant differences in group outcomes for exercise oximetry (2% difference) and gas transfer factor (0.4 ml/minute/kPa). Oximetry was expected to require the smallest numbers compared to the other outcome measures in the study.

Table 3.1 Sample size estimation for different outcome measures

Outcome (units)	Estimated * difference	SD #	n per group $
Respiratory Symptoms (%)	50		82
	100		26
FVC (l)	0.2	0.55	95
	0.3	0.55	42
K_{co} (ml/min/kPa)	0.4	0.73	42
Desaturation (%)	2	2	17

* Estimated difference in means or risk ratio between control and exposed groups.

Standard deviation (used for both control and exposed groups) estimated from the literature.

$ Two sample one sided estimation

3.3 Measurement of Exposure

3.3.1 Estimation of occupational exposure to pesticides

Documentation of past exposures to specific pesticides in South Africa are not available. Data on pesticides sales are not good proxies for usage patterns due to different costs of pesticides. Data on the amounts of pesticides sold and bio-equivalents are difficult to extrapolate to individual levels due to a lack of information on the number of sprayers and the different ways in which sprayers might be exposed in an occupational setting. Detailed industrial hygiene measurements of workplace chemicals in the working environment or biological monitoring data are absent.

Estimation of exposure by means of job exposure matrices

A number of researchers have developed the concept of a job exposure matrix (JEM) as a low cost and systematic method for estimating individual exposures to chemicals (2, 3). This concept has been refined and applied to agricultural settings (4-7). A job exposure matrix is based on job history variables which are used to calculate individual chemical exposures of workers. The job history variables include aspects of job activity such as job title or calender year, which can be used to estimate chemical exposures, for example different calender periods can represent different degrees of exposure according to

the history of chemical usage patterns in the area. JEMs are used in combination with job duration to calculate long term exposure. A JEM has value in an agricultural setting where the subjects's recall of job activity exceeds their ability to recall specific chemical exposure information (4-5). This is particularly true where education levels are low.

Recently, Daures (6) used an agricultural JEM based on calender year of spraying activity and farm location to estimate pesticide exposure amongst French vine farmers. The JEM was combined with agrochemical-specific data on application method, duration of application, hectarage and applied quantities to estimate cumulative exposure to a specific agrochemical. In another study, Migli (5) used a similar JEM which also included the type of crop production. The JEMs in both studies were validated against an assessment by agricultural experts. However, both researchers indicated the need for further validation with methods which measured pesticide exposure directly. Later studies used personal protective equipment (7), method of application (7) and the type of crop production in JEM's to estimate pesticide exposure (4).

The JEM in the core study :

The core study (1) drew on the above models to develop a JEM based on specific activities performed in a particular job and crop sector (pomefruit, stone fruit, etc) to estimate exposure to organophosphate pesticides. The highest exposure activity

(indoor mixing) was weighted 1 and other less exposed activities (such as outdoor mixing, back - and hand spraying and tractor spraying) were weighted relative to this exposure. Indoor mixing was considered to be the most exposed job activity because of exposures to concentrated pesticide solutions indoors. Spraying activities were weighted lower due to exposure to less concentrated solutions. This information was obtained from extensive interviews with industry (1) and the job rating was "validated" by consulting key informants in the industry using the Delphi technique. Crop sector weights were based on the concentration of organophosphates per hectare applied in that sector.

The JEM in the current study:

Because of the predominance of pome fruit farming in the core study, farming was assumed to be in one crop for this study. Less environmental exposure results from herbicide spraying which is directed downward compared to insecticide spraying which is directed upward and therefore the JEM used in the core study which concerned organophosphate (insecticide) exposure was modified for use in the current study which concerned paraquat (herbicide) exposure. The modifications were:

i) a reduction in the number of exposure activities
ii) the weighting of tractor driving less than hand- and backspaying.

The JEM used for the calculation of individual paraquat exposures provided the following exposure intensity weights expressed relative to a maximum value of 1 for the highest possible job exposure:

mixing indoors:	1.0
mixing outdoors :	0.8
backspray or handspray :	0.7
tractor driving:	0.5
repair of herbicide equipment:	0.2
gardening:	0.05
other exposures	0.05

3.3.2 Exposure Questionnaire (refer to appendix 1.2 and 1.3):

The job history questionnaires, which were specially developed, included separate exposure items for each agricultural job performed (the last 10 agricultural jobs performed). This included the type of farming product, employment period and type, and exposure mechanism (mixing, tractor spraying, hand spraying, back spraying, repair of spray equipment, gardening. The worker was asked to estimate the duration of specific exposure activities (refer to table A in appendix 1.2). The direction of spraying upwards or downwards, indicated insecticide spraying or herbicide spraying respectively.[1] Paraquat exposure was specifically recorded including information about skin burns, and

[1] Items marked "A" in appendix 1.2 and 1.3

specific product brandnames (paraquat, gramazone and preeglone).[2] Short-term exposure was measured from exposure in the previous 13 months (one season)[3]. Previous pesticide poisoning occurrence and severity history was obtained[4].

3.3.3 Calculation of variables

Total long term cumulative exposure indices for herbicides (HERBACE , those spraying herbicides in general) and paraquat (PARACE, those who sprayed paraquat as the herbicide) were calculated by multiplying the total number of days accumulated in individual exposure tasks by the weight for that task from the JEM and summing all exposures across all jobs. A simple example:

A worker was employed as a paraquat backpack sprayer and mixer (indoors) for 5 years, working on average for 6 months per year and 5 days a week (660 days), in his first job. In his second job he worked for 2 years, 5 months per year and 3 days per week as a tractor sprayer of paraquat (126 days). His total cumulative paraquat exposure during the two jobs is:

1st job mixing :

660 days X 1 (JEM weight for indoor mixing) = 660 JEM days

---

[2] Items marked "B" in appendix 1.3

[3] Table marked "C" in appendix 1.3

[4] Item marked "D" in appendix 1.2

1st job spraying:

660 days X 0.7 (JEM weight for spraying) = 462 JEM days

2nd job spraying:

126 days X 0.5 (JEM weight for tractor spraying) = 63 JEM days

Total cumulative paraquat exposure for 2 jobs

= 660 + 462 + 63 JEM days

Since workers may be involved in different activities in different, and even the same farm jobs, exposures may be summed over time to derive cumulative and average lifetime intensity exposure estimates (8).

Lifetime average intensity of herbicide (HERBINT) and paraquat exposure (PARINT) were calculated by dividing total cumulative exposure indices by the total period of employment.
Short-term exposure (SHERBACE, SPARACE) indices were calculated from exposure in the previous 13 months. Pure long-term exposure variables (PARACE2, HERBACE2, PARINT2, HERBINT2) were calculated by subtracting short-term exposure from long-term cumulative exposure (for example PARACE2 = PARACE - SPARACE).

Short- and long- term exposure were dichotomised to form a number of categorical exposure variables using different cutpoints (0,25th,50th and 75th percentiles). An ordinal long-term exposure variable with 4 categories (variable EXGRAD listed in

glossary, appendix 4) was created based on the dichotomised exposure variables.

Current exposure status used for sampling was thus not used in the analysis of the data.

3.4 Measurement of Respiratory Health

3.4.1 Medical Examination

A directed medical examination including chest radiography was carried out by a doctor to exclude cases of tuberculosis. One subject was diagnosed as having tuberculosis and therefore did not perform the clinical tests.

3.4.2 Respiratory Questionnaire

Respiratory symptoms were measured using a vernacular version of the American Thoracic Society (ATS) respiratory symptoms questionnaire modified for SA conditions (9, appendix 1.4). The items included in the questionnaire were coughing, production of phlegm, shortness of breath, wheezing and chest-tightness in increasing degrees of severity, as well as past history of respiratory illness including bronchitis, pneumonia, hayfever, sinus problems, asthma and tuberculosis.

The ATS questionnaire has been found to be more detailed than the questionnaires developed by the British Medical Research Council

and The American National Heart and Lung Institute while eliciting similar response rates and symptom prevalences (10, 11). The questionnaire has also been found to be valid (10), and correlates with spirometric measurements (12). It can be used to predict both restrictive and obstructive defects.

3.4.3 Lung function

Lung function testing included spirometry for the detection of ventilatory impairment, and measurement of the transfer factor for the detection of impairment at the gas exchange level.

Spirometry:

Spirometry involves the measurement of dynamic lung volumes and flow rates during forced inspiration and expiration or forced breathing when maximal effort is applied throughout the manoeuvre. The information is mostly obtained in terms of the relationships of inspired or expired volumes to time which are described by the volume time curve or relationship of maximal flow rate to lung volume described by flow-volume curve (the lung function report sheet in appendix 2 include an example of the flow-volume curve).

Transfer factor:

The test is used to assess the transfer of gases between the alveoli and the capillaries. The high permeability of the

intervening membrane to carbon monoxide and the similar molecular weight of CO and O_2, makes this gas suitable for this measurement.

The test is based on measuring the difference in carbon monoxide concentration in inspired and expired air before and after a 10 second breathhold. A test gas which is low in carbon monoxide and includes an inert gas not normally present in the body (eg helium) is inhaled at nearly full functional capacity and held in the lungs for 10 seconds. A sample of alveolar gas is obtained during exhalation and analyzed for both gases. The dilution factor for helium is then used to calculate the initial carbon monoxide concentration in alveolar gas and to estimate alveolar volume.

The transfer factor is determined mostly by the diffusing capacity of CO and its binding to haemoglobin.

Equation used for the calculation of transfer factor:

$$T_{LCO} = VA\ (STPD)\ X\ 60/t\ X\ 1/(PB-47)\ X\ \ln COA/COE$$

T_{LCO} = Single breathe diffusing capacity for CO

$K_{CO} = T_{LCO}/VA$

VA = Alveolar volume (STPD) at which breath was held (Calculated from helium dilution)

t = Breathe holding time in seconds

PB = Barometric pressure

COA & COE = Initial and expired alveolar [CO]

(Initial alveolar [CO] calculated from helium dilution)

Measurement of lung function:

Spirometry and carbon monoxide gas transfer measurement were performed using the Medical Graphics PF/D/x Pulmonary Functions Test System (Medical Graphics Corporation, USA). The tests were performed by a trained respiratory health technologist according to ATS criteria (9). The equipment was recalibrated after each work session. Parameters (refer to appendix 2) included height, weight, body surface area, forced expired vital capacity (FVC), forced one second expiratory volume (FEV1), the ratio of FEV1 to FVC (FEV1/FVC), forced maximum expired flow rate (FEFMAX), and transfer factor uncorrected T_{Lco}) and corrected for alveolar volume (K_{co}). Transfer factor was not corrected for haemoglobin because the procedure involving this measurement is invasive and this might have affected participation of subjects in the study. The small amount of bias which might have resulted from this is expected to be non-differential.

Predicted and percentage of predicted values were calculated for spirometry and transfer factor from the European Community for Coal and Steel standard reference values (13) because:

i) they are recommended by the ATS

ii) they have values for a number of important parameters that cold be measured in addition to spirometry

iii) they are widely available on software

iv) with experience we have some idea of how they relate to RSA.

3.4.4 Radiography

Standard PA chest radiographs were taken by two trained radiographers at Ceres Hospital and were read by a doctor[5] according to the standard in the International Labour Organisation (ILO) International Classification of radiographs of pneumoconioses (1980) (14).

3.4.5 Exercise Testing

A modified standard clinical stage one exercise test was performed by myself. This involved the measurement of arterial oxygen saturation by means of oximetry (Ohmeda Biox 3700) during an incremental exercise test performed to exhaustion on a mechanical Monark cycle ergometer.

The exercise test involved cycling at 50 cycles per minute (following the sound of a metronome) while the work rate was increased every minute by 100 kilopondmetres per min (kpm/min, 1 kilopondmetre = 9.8 Joules), starting at 600 kpm/min after an initial 1-2 minute warm-up. Earlobe oximetry was predominantly used, but in two cases finger oximetry was used because earlobe oximetry was unsuccessful. Vaso-dilating ointment (Salicylic acid) was applied to improve blood circulation and improve

[5] Neil White

measurement by the oximeter. The oximeter was connected by serial connection to an IBM compatible computer which captured data every two seconds after subjects' resting saturation levels stabilised. Pulse rate was also recorded. Workloads performed by subjects, exercise durations, as well as pre- and post-exercise saturation and pulse rate were also recorded.

Traces of pulse-rate and saturation against time were plotted from the recorded values (Appendix 3). The starting time of exercise relative to the point at which computer recording started was indicated by the increase in heart-rate from resting values (the duration of the warm up as indicated by the traces was confirmed by manual records) and the end of exercise was indicated by the drop in heart rate after exercise (confirmed by manual records). Heart rate and saturation levels at specific work loads could thus be determined. Irregular and inconsistent heart and saturation traces were considered to be uninterpretable and were therefore excluded from the analysis. Appendix 3 shows examples of interpretable and uninterpretable traces.

Desaturation was calculated as the difference between resting and maximum exercise saturation levels. Desaturation was dichotomised to form a number of categorical outcome variables using different cutpoints ($\geq$ 1%, $\geq$ 2%, $\geq$ 3%, $\geq$ 4% and $\geq$ 5%). Predictions of heart rate and workload used were those of Campbell and Jones (15):

Maximum predicted heartrate (beats/min) = 210 - (0.65 X age)

Maximum predicted workload (MPW):

MPW (kpm/min) = {[(60 - 0.55 X age)weight]-(3.5 X weight)}/2

Conversion of workload (WL) to oxygen consumption (V02):

V02 (ml/min) = (WL X 2) + (3.5 X weight)

* Units: WL - kpm/min; age - years; weight - kg

3.5 Possible confounders or effect modifiers

Age, smoking, gender, social class and body size are known predictors of respiratory health measured by spirometry, diffusion capacity and oximetry (17-24). All subjects in the study sample were males. Social class was considered to be homogeneous in the study sample because all subjects could be classified as belonging to the same income group. The study also included measurements of weight and height (performed before lung function testing) which could be used as indices of body size. The study included measurement of alcohol because of the history of high consumption levels in rural areas. Alcohol has been linked to survival from severe paraquat intoxication in heavy drinkers (25). Education could influence the workers ability to performance in tests and answer questions.

Education history, alcohol consumption and smoking history were obtained by questionnaire (appendix 1.1).

Years of schooling was used as proxy for education.
Life time alcohol consumption (grams) was determined from daily

drinking patterns, lifetime period of drinking and the amount of alcohol consumed. Quantities and qualities of beverages and tobacco were obtained from sample containers on display. Smoking was measured in 20 cigarette pack-year equivalents. Smoking and alcohol were dichotomised to form categorical confounder variables (listed in glossary, appendix 4).

3.6 Field work

All questionnaires were tested in a pilot of 10 subjects.

Data was collected at the Ceres Hospital during the last two weeks of May 1994. Subjects were directed to various measurement stations (X-ray, interview, pulmonary function and exercise test) by two supervisors. Quality control included a checklist on envelopes, colour coding of questionnaires and the checking of completed questionnaires by the supervisors. The recording of exposure information was performed before the pulmonary function tests, exercise tests and administration of the respiratory symptom questionnaires and observers for each station were blind to the results from other stations.

All questionnaires were in Afrikaans (vernacular language) and administered by trained interviewers.

3.7 Ethical considerations

All workers who participated in the study gave written consent after full explanation of the purpose and methods of the investigation. This was done in accordance with the Declaration of Helsinki of the 25th World Medical Assembly (WHO, 1982), and transacted in Afrikaans, the first language of the subjects.

Full confidentiality was observed for the subjects.

3.8 Data management

Data was encoded by one person and double punched by the University of Cape Town data capture service. Statistical analysis was conducted on a mainframe VAX computer at UCT using SAS 6.09.

3.9 Statistical Analysis

3.9.1 Univariate analysis

The data was cleaned by inspecting outliers using the PROC FREQ and PROC UNIVARIATE procedures in SAS.

The distributions of all the continuous variables included in the analyses were examined for normality by running the PROC UNIVARIATE PROCEDURE in SAS and this included inspection for symmetry using stem-and- leaf and box-plots, observation of the

closeness of the mean to the median and by the Shapiro-Wilk test for normality. Non-normally distributed variables were transformed where appropriate for purposes of bivariate and multivariate analyses.

3.9.2 Bivariate analysis

Bivariate analyses were used to explore associations between relevant outcome and predictor variables and to assess likely confounding with a view to building models for multivariate analysis which included multiple linear and logistic regression techniques.

Table 3.2 summarises the bivariate tests used for detecting associations and table 3.3 summarises the associations examined.

Table 3.2 Summary of bivariate tests performed

variable type	categorical	continuous
categorical	Chi-square Test	T-test (parametric) Wilcoxon Test (non-parametric)
continuous		Pearson correlation Coefficient (parametric) Spearman Rank Correlation Coefficient (non-parametric)

Table 3.3 Associations examined

variable	outcome	exposure	possible confounders and effect modifiers
outcome	association of outcome measurements	Measures of effect	independent predictors of outcome
exposure	Measures of effect	association of exposure variables	correlation of potential confounders with exposure

3.9.3 Multivariate Analysis

Multivariate analysis included multiple linear regression and multiple logistic regression procedures. A model was constructed for each outcome. Regression diagnostics were performed to ensure that the assumptions underlying linear regression were met. Models results were examined for homoscedasticity of residuals and any obviously non linear relationships.

Model Selection:

Multivariate models included a priori variables known or thought likely to be associated with outcomes of interest.

i) Age, height and weight, smoking and alcohol consumption were included in all outcome/exposure models as possible confounders. Both height and weight were included in most models as proxies of body size, but for statistical stability, only one (the strongest bivariate and multivariate predictor) was included where the number of data points were below 100.

For exercise desaturation, difference in post exercise and resting heartrate were included to control for exercise exertion.

ii) Other variables found in the bivariate analysis to be associated (p-value = 0.2) with the outcome or with important exposure or a priori variables (potential confounders) were also included.

Collinearity between selected variables was examined in order to prevent simultaneous inclusion of strongly correlated variables in the model. Variables showing strong collinearity ($r \geq 0.8$) were run independently in the model and the variable with the strongest association was included in the model.

Individual predictors rather than ratios of predictors were included in models, for example FEV1 and FVC rather than the FEV1/FVC ratio were analyzed as outcomes, and weight and height were included individually rather than the body mass index ratio.

Modelling procedures:

Regression was performed using the PROC REG AND PROC LOGISTIC procedures in SAS. Significant associations between variables were assessed from full model procedures. For lung function and exercise oximetry the best explanatory models were assessed by running stepwise, forward and backward stepping and the C_p (based on Mallows C_p statistic) procedures in SAS.

Descriptions of selection procedures:

Full model procedure: All predictors are forced in the model.

Forward selection procedure: Selected predictors are added one by one to the model in the order of the magnitude of their contribution (F to enter statistic corresponding to $p < 0.1$) to the model. Variables are not included if they do not exceed a specified F to enter - statistic. Variables stay in the model once they are included.

Backward Procedure:

The backward procedure involves the elimination of individual predictors from the full model starting with the variable with the lowest contribution to the model. Elimination stops when the remaining model exceeds a specified model statistic (F to enter statistic corresponding to $p < 0.1$).

The Stepwise Procedure:

This is a modification of the Forward Selection Procedure. Variables are included in the model as in Forward Selection but at each inclusion the contributions of all the variables in the model at that stage is assessed and elimination occurs as in the Backward Procedure.

The C_p procedure:

All possible subsets are listed in order of ascending C_p statistic values. The C_p statistic (24) gives an indication of the loss in predictive power of models. The model with the

lowest C_p value and explaining most of the variance (high model r^2) is the best explanatory model.

All datapoints including outliers were analyzed.

Possible effect modification

Possible effect modification was studied by including interaction variables (exposure X effect modifier) as predictors in models. The full model and all stepwise procedures were used. A variable was considered an effect modifier if the interaction variable was a significant predictor in the full model of the outcome of interest.

Relationship between lung function and oximetry

The relationship between lung function and oximetry was investigated by including desaturation as a predictor in the linear regression models for FEV1, FVC, and diffusion capacity.

3.10 References

1. London L, An investigation into the neurological and neurobehavioural effects of long-term agrochemical exposure among deciduous fruit farm workers in the Western Cape, South Africa,1994 [MD Thesis]. Cape Town: Department of Community Health. University of Cape Town, 1994.

2. Hoar SK, Morrison AS, Cole P, Silverman, DT. An occupational and exposure linkage system for the study of occupational carcinogenesis. Journal of Occupational Medicine 1980; 22: 722-725

3. Pannet B, Coggon D, Acheson ED. A job-exposure matrix for use in populations based studies in England and Wales. British Journal of Medicine 1985; 42: 777 - 783

4. Nanni O, Ricci M, Lugaresi C, Amadori D, Falcini F, Buiatti E. Interactive use of a priori exposure matrix to improve the characterisation of chemical exposures in agricultural work studies. Scandanavian Journal of Work and Environmental Health 1993; 19: 191 - 199

5. Migli L, Settimi L, Masala G, Maiozzi P, Alberghinin Maltoni S, Seniori Constantini A, Vineis P. Pesticide exposure assessment: a crop exposure matrix. International Journal of Epidemiology. 1993; 2(6) Suppl 2: S42 - 45

6. Daures JP, Momas I, Bernon J, Gremy F. A vine-growing exposure matrix in the Herault Area of France. International Journal of Epidemiology 1993; 22(6) Suppl 2: S36 - 41

7. Brouwer DH, Brouwer EJ, Van Hemmen JJ. Estimation of long-term exposure to pesticides. American Journal of Industrial Medicine. 1994; 25: 573 - 588

8. Checkoway H, Pearce N, Crawford - Brown DJ. Research methods in occupational epidemiology. Oxford University Press 1989. Oxford

9. Ferris GB. Epidemiology Standardization Project. American Review of Respiratory Disease 1978; 118: 1-35

10. Helsing J K, Comstock GW, Speizer FE, Ferris BG, Lebowitz MD, Tockman, Burrows B. Respiratory symptoms. American Review of Respir Disease 1979; 120; 1221 - 1230

11. Comstock G, Tockman MS, Helsing JK, Hennesy KM. Comparison of the old and the new. American Review of Repiratory Desease 1979; 119; 45 - 51

12. Brodkin CA, Barnhart S, Anderson G, Checkoway H, Omenn GS, Rosenstock L. Correlation between respiratory symptoms and pulmonary function in asbestos-exposed workers. American Review of respiratory Disease 1993; 148: 32 - 37

13. European Community for Coal and Steel.
Bulletin European de Physiolopathogie Respiratoire 1983; 19 Suppl 5: 7-95.

14. White N, Ehrlich R, Rees D. A guide to spirometry as applied to occupational health. South African Medical Journal 1996; 86: 807 - 813

15. International Labor Office: Guidelines for the use of ILO international classification of radiographs of pneumoconioses. Geneva: International Labour Office,1980

16. Jones NL, Campbell EJM. Clinical exercise testing. 2nd ed. Philadelphia: W.B Saunders, 1982.

17. Samet JM, Schrag SD, Howard CA, Key RC, Pathak RD. Respiratory disease in a New Mexico Population sample of Hispanic and non-Hispanic whites. American Review of Repiratory Desease 1982; 125: 152 - 157

18. Beck G, Doyle CA, Schachter EN. Smoking and lung function. American Review of Repiratory Desease 1981; 123: 149 - 155

19. Senthilselvan A, Chen Y, Dosman JA. Predictors of asthma and wheezing in adults: grain farming, sex, and smoking. American Review of Repiratory Desease 1993; 148: 667 - 70

20. Iversen M, Dahl R, Korsgaard J, Hallas T, Jensen EJ.

Respiratory symptoms in Danish farmers: an epidemiological study of risk factors. Thorax 1988; 43: 872 - 877

21. White NW, Hanley JH, Lalloo UG, Becklake MR. Review and analysis of variation between spirometric values reported in 29 studies of healthy African Adults. American Journal of Respiratory and Critical Care Medicine 1994; 150:358 - 55

22. Gamsky TE, Mccurdy SA, Samuels SJ, Schenker MB. Reduced FVC among California grape workers. American Review of Repiratory Desease 1992; 145: 257 - 262.

23. Hansen JE, Sue DY, Wasserman K. Predicted values for clinical exercise testing. American Review of Repiratory Desease 1984; 129 Suppl: S49 -S55

24. Comstock GW, Meyer B, Helsing KJ, Tockman MS. Respiratory effects of household exposures to tobacco smoke and gas cooking. American Review of Repiratory Desease 1981; 124: 143 -148

25. Ragoucy-Sengler C, Pileire B, Daijardin JB. Survival from severe paraquat intoxication in heavy drinkers. Lancet 1991; 338: 1461.

25. Mallows CL. Some Comments on C_P. Technometrics 1973; 15 : 661 - 675

CHAPTER 4 RESULTS

4.1 Univariate Analysis

4.1.1 Sample participation, demographics and anthropometry

Of farms agreeing to participate when contacted, 41 (100%) were studied. This represents 34.7% of the farms in the study region. Of workers selected, 126 (95%) including all current herbicide sprayers (62) were studied.

Table 4.1 shows a low education level (7.2 ± 3.57 years) with 12.7% never attending school. Height and weight measurements (Table 4.1) were low compared with ECCS reference populations (1)

Table 4.1 Anthropometric results in the study sample

Variables (units)	Mean	SD	n	Range
Education (yrs)	7.2	3.57	126	0-14
Weight (Kg)	56.1	8.9	125	35 - 85
Height (cm)	163.6	6.9	125	147 - 177
Age (years)	34.2	9.9	126	18 - 65

Note: n = 126 where information was obtained for all subjects, but n = 125 where tuberculosis case was excluded.

4.1.2 Respiratory symptoms and illnesses

A summary of important respiratory symptom prevalences is shown in table 4.2 (Appendix 5.1, table 2 lists all respiratory symptom prevalences measured).

Table 4.2

Respiratory symptom prevalences

Variable	Prevalence (%) n=126
Regular coughing	57.1
> 3 mnths	11.9
> 2 years	7.9
Production of phlegm during coughing	32.5
> 3 mnths	10.3
> 2 yrs	7.9
Coughing and phlegm > 3wks	23.8
> 2 years	21.4
Wheezing in past year	46.8
Shortness of breath during wheezing (SOBW)	25.4
Awake in morning due to SOBW	7.9
Attack of SOBW	8
Medication received for SOBW	2.4
Wheezing for > 2 years	22.2
Dyspnea during fast or incline walking	40.5
Slower walk than people of same age	15.9
Dyspnea during level walking	7.9
Dyspnea during level walking for 100m	7.1
Get colds in chest	75.4
Severe chest colds in past 3 yrs	15.9
Phlegm during chest colds	11.9

Table 4.3 shows a summary of important respiratory illness prevalences (Appendix 5.1, table 2 lists a all respiratory illness prevalences measured).

Table 4.3

History of Respiratory illness

Variable	Prevalence (%) n=126
Lung problems before 16	9.5
Bronchitis	16.7
Pneumonia	21.4
Hayfever	14.3
Sinus problems	19.0
Tuberculosis	7.9
Asthma	2.4

4.1.3 Radiography

The prevalence of past and present x-ray evidence of tuberculosis was 5.6%. Prevalence of small opacities (≤ 1/0), was 17.6%, with 1/0 being the highest score.

4.1.4 Respiratory Function

A summary of important respiratory function test results are given in table 4.4 (Appendix 5.1, table 1 gives a summary of all

respiratory function results). Lung capacities are consistently 10 - 15% lower than ECCS reference values, while lung diffusion capacities are higher than ECCS reference values (All lung function values were significantly different from ECCS reference values [1]).

Table 4.4

Lung Function values

Outcome (units)	Mean	SD	n	% of ECCS reference
Forced Vital Capacity (FVC,l)	3.73+	0.61	125	89.24
Forced 1-second Expiratory Volume (FEV1,l)	3.06+	0.57	125	86.11
FEV1/FVC(%)	82.03+	9.84	125	96.85
Forced expiratory flowrate (l/sec)	7.73+	1.91	125	89.23
Transfer factor (T_{LCO}, ml/min/kPa)	4.10+	0.75	107*	106.4
T_{LCO} /alveolar volume (ml/min/kPa/l)	0.78+	0.14	107*	117.12

* n = 107 for measurement of transfer factor due to breakdown of gas analyzers on day 6 of fieldwork.

+ Mean is significantly ($p < 0.05$) different from ECCS reference value (1).

4.1.5 Exercise Test

A summary of important exercise test outcomes are shown in table 4.5 (Appendix 5.1, table 1 gives all the univariate exercise test results).

Table 4.5

Exercise test results

Outcome (units)	Median	Mean	SD	n*	Range
Maximum work Load (MWL, Kpm/min)		1080.3	164.46	122	700 - 1500
% predicted MWL		103.45	19.80	122	59 - 170
Resting saturation (%)		98.3	1.5	90	95 - 100
Saturation at MWL (%)		95.8	2.7	90	86 - 100
Difference in saturation(%)		2.54	2.36	90	-1 - 10
Rest. heart rate (beats/min)	65	68.8	15.2	122	60 - 120
Maximum heart rate (beats/min)	170	168.7	12.2	122	137 - 200
Difference in heart rate (beats/min)	101.5	99.9	16.52	122	32 - 132
% of predicted maximum heart rate		89.6	6.65	122	73 - 104
VO_2MAX (ml/min)		2357.9	335.6	122	1582 - 3210

Medians are given for non-normally distributed variables

* n = 122 for total exercise tests completed; n = 90 for number of

One hundred and twenty - two subjects performed the exercise test and 90 saturation traces in this group were considered interpretable. The proportion of traces that were considered unintepretable was 28.6%. This group of subjects did not differ significantly from the group with interpretable traces with respect to age, schooling years, maximum heartrate, smoking history, alcohol consumption and lifetime paraquat exposure, but was found to be significantly shorter and lighter ($p < 0.05$). This group also had significantly lower prevalences of chest illnesses and colds ($p < 0.05$).

The prevalence of desaturation at different cut-off levels was 73.3% for ≥ 1%, 32.2% for ≥ 4% and 18.8% for ≥ 5% cut-off levels.

Table 4.5 shows the average maximum workload attained to be 1080.3 kpm/min or 103.5% of predicted, corresponding to a V02max of 2.36 l/min. This suggests that most of the subjects where exercising at their true maximal potential. The average maximum pulse rate was 89.6% of predicted values.

4.1.6 Life style factors

Median 20 cigarette pack-years was 7.5 (range = 0-94.5). Lifetime alcohol consumption was 148.8 kg (range = 0-1298.7). Prevalences of lifetime alcohol (92.9 % more than 1 gram) and smoking (84.8% smoked more than 1 cigarette pack-year) consumption are high. Smoking information for one subject was

excluded due to inconsistent questionnaire responses.

4.1.7 Exposure

Table 4.6 shows a summary of important exposure indices (Appendix 5.1 table 1 gives a full summary of exposure values).

Table 4.6

Exposure univariate results

Exposure (units)	Median	n	Range
Employment (years)	16.0	126	3.0 - 54.0
Lifetime average intensity of paraquat exposure (days/yr, JEM* units)	12.81	68′	0.07 - 192.36
Total cumulative lifetime paraquat exposure (JEM* days)	190.3	68′	1.8 - 5196
Short-term exposure (JEM* days)	45.0	41′	0.7 - 135

* JEM = Job Exposure Matrix (see methods)

′ n of those exposed > 0 JEM days (numbers < 126)

The average total cumulative exposure of the paraquat exposed workers in the study was found to be approximately 0.52 JEM year-equivalents. The average number of years employed in exposed jobs in this particular group of workers was 11.5 years (range 1 to 47).

No subject reported having been previously poisoned by paraquat.

Only four subjects, of whom 3 had interpretable saturation traces in exercise testing, reported past history of skin burns (back, hands or other) due to paraquat use. The average desaturation in these subjects was 4.67 ± 5.03%.

4.2 Bivariate analyses

All categorical and continuous variables (listed in glossary in Appendix 4) were used to explore associations of interest (based on table 3.3 in Methods) using the appropriate statistical tests.

Appendix 5.2 lists the significant associations found in bivariate analysis. For simplicity, only the associations of effect involving total cumulative exposure as index for long term exposure are shown. Similar associations were found for average lifetime intensity indices.

Important associations:

i) Exposure effects on different outcomes:

Oximetry (associations marked "a" in appendix 5.2):

The degree of desaturation was positively associated with highly exposed (EXPA700, EXPPA700) and recently exposed (EXPS, EXPP, SPARACE, SHERBACE) subjects.

Reported respiratory health (associations marked "b" in appendix 5.2):

Past history of phlegm production and episodes of coughing and phlegm were associated with exposure (EXPA0, EXPA50, EXPA100, EXPPA100, EXPPA250), and wheezing with highly exposed subjects (EXPA700, EXPPA700).

ii) Associations between potential confounders and outcome indices:

Smoking (NICCAT) was associated positively with past history of coughing (associations marked "c" in appendix 5.2).
Age (AGE), weight (WEIGHTKG) and height (HEIGHTCM) were associated with most lung function indices (associations marked "d" in appendix 5.2).

iii) As expected, exposure (EXPA700) was positively associated with age (association marked "e" in appendix 5.2). Exposure (EXPPA250, EXPPA700) was also positively associated with alcohol consumption (association marked "f" in appendix 5.2).

4.3 Multivariate Analysis

Bivariate analysis of the study data did not produce additional variables for inclusion in multivariate models in addition to those already included on theoretical grounds.

Smoking and alcohol were treated as continuous variables in all models, because of the low prevalence of non-smokers and non-alcohol users (refer to univariate results).

Long-term exposure variables were run in separate models due to collinearity (> 0.9). Short-term exposure was run i) alone as an independent exposure variable in models and ii) together with total long-term exposure as separate predictors in models. The effects of all exposure indices on all outcomes were analyzed.

Because of the similarity of results for radiography, respiratory symptoms and lung function when a) using total long-term measures (includes short-term exposure for example PARACE) for herbicides or paraquat b) using pure long-term measures (long-term exposure after subtraction of short-term component for example PARACE2) and c) including short-term exposure measures in models as described above, the results of only one exposure index (total cumulative exposure) is illustrated below for each outcome.

4.3.1 Radiographic results

No significant associations were found between small opacity profusion score and age, weight, height, alcohol, smoking and exposure (table 1 in appendix 5.3 summarises the full models when using total cumulative paraquat exposure as an exposure index).

4.3.2 Respiratory Symptoms

None of the reported respiratory symptoms were significantly related to paraquat exposure, neither were they consistently related to any of the other predictors in models which included age, weight, height, education, smoking and alcohol (Appendix 5.4 Table 1 summarises the full models when using total cumulative paraquat exposure as an exposure index).

4.3.3 Respiratory Function Tests

Appendix 5.5, table 1 summarises the linear regression analysis for lung function when using total cumulative paraquat exposure as an exposure index.

Height, weight and age were significant predictors explaining most of the variance for most respiratory function outcomes and were the variables included in the models with the lowest C_p. Alcohol (adjusted ß = 5.4×10^{-6} % per g, SE(ß) = 2.5×10^{-6} % per g, p = 0.03) was found to be a significant predictor of diffusion capacity and was included in the model with the lowest C_p.

Smoking was not a consistent predictor and exposure did not significantly affect respiratory function. Only maximum expiratory flow-rate (FEFMAX) was significantly associated with exposure (ß = 5.2 x 10-4 l/sec, SE(ß) = 2.4 x 10-4 l/sec, p = 0.031).

Table 4.7 lists full model regression equations for spirometry in which a) significant predictors found in our study are listed and b) for comparison with the literature only height and weight are included.

Table 4.7

Full model regression equations for spirometry when including a) only significant predictors found in our study and b) only height and age

Equation	R_2	p-value
a) FVC = -2.62 - 0.021 AGE + 0.08 WEIGHT + 0.04 HEIGHT	0.3	0.0001
b) FVC = -3.25 - 0.019 AGE + 0.047 HEIGHT	0.3	0.0001
a) FEV1 = -0.069 - 0.029 AGE + 0.017 WEIGHT + 0.019 HEIGHT	0.39	0.0001
b) FEV1 = -1.35 -0.025 AGE + 0.03 HEIGHT	0.34	0.0001

4.3.4 Exercise Test Results

Weight, age and difference between post- and pre-exercise heart rate were significant predictors for maximum work load (MAXWL) achieved in exercise testing in a model that also included smoking, alcohol, oxygen saturation at rest and total cumulative paraquat exposure. (Appendix 5.6, table 1 summarises multivariate results).

Exercise oxygen desaturation

Diagnostics for linear regression and procedure of multivariate analysis:

The Shapiro-Wilk test (a stringent test) for normality indicated that the residuals were not normal. A number of attempted transformations did not improve normality. Stem and leaf and box plots, however did indicate near-normality and because of its robustness, multiple linear regression (statistical notes: Department of Statistics, UCT) was used for exercise desaturation models. Model results were examined for homoscedasticity of residuals and any obviously non linear relationships. Additionally, the nature of potential associations were examined by logistic regression. For logistic regression, dichotomised outcome variables (listed in glossary, appendix 4) were modelled with continuous and dichotomised paraquat exposure variables.

Correlation matrix:

The correlation matrix of the full model (Appendix 5.7) indicated that collinearity between variables was not a problem (all $r < 0.8$).

Variables selected:

Table 4.8a summarises the full model results for the relationship between exercise oxygen desaturation and long-term paraquat exposure, using lifetime average intensity of exposure, which had the strongest effect, as an exposure index. Long-term paraquat exposure (partial $r^2 = 0.0652$; $p = 0.019$) and weight (partial $r^2 = 0.0431$; $p = 0.027$) were significant predictors of exercise oxygen desaturation although this explained only a small proportion of the variance. The unadjusted regression coefficients were :

WEIGHTKG: -0.0459 % desaturation/kg ($r^2 = 0.0326$, $p = 0.0887$)

PARINT: 0.0176 % desaturation/JEM day/yr ($r^2 = 0.057$, $p = 0.0232$)

Exposure and weight were also the only variables selected in stepwise procedures and in the model with the lowest C_p (Table 4.8b)

Table 4.8 Two multiple linear regression models for the effect of lifetime average intensity of paraquat exposure on exercise oxygen desaturation.

a) Full Model (n = 90, C_p = 7.000)

Predictor	ß	SE(ß)	P-value	Partial. R2
AGE (yrs)	0.0350	0.03033	0.252	0.0007
WEIGHT (kg)	-0.0620	0.02760	0.027	0.0431
SMOKE (pckyrs)	0.0067	0.01787	0.710	0.0012
ALCOHOL (kg)	-6.74×10^{-6}	1.55×10^{-6}	0.666	0.0026
DIFFHR (bts/min)	0.01499	0.01754	0.395	0.0140
PARINT (days/yr)	0.0194	0.00811	0.0190	0.0652

Model R^2 = 0.1222 (DF=6, p = 0.090)

b) Best Model resulting from stepping and Cp procedures in SAS (n = 90, C_p = 0.894)

Predictor	ß	SE(ß)	P-value	Partial R^2
WEIGHT	-0.0514	0.0260	0.051	0.0408
PARINT	0.0186	0.0075	0.015	0.0611

Model R^2 = 0.1019 (DF = 2, p = 0.010)

Similar results were found when using a) total long-term exposure measures including lifetime average intensity and lifetime cumulative herbicide or paraquat exposure b) pure long-term exposure measures. Average intensity of exposure was the strongest predictor. PARINT which is a measure of total long-term exposure was used for illustrative purposes in table 4.8. Table 4.9 which gives a summary of linear regression associations with exposure variables, illustrates these effects. The linear regression exposure results were also supported by logistic regression results of the same relationships as well as that between dichotomised exposure and dichotomised oxygen desaturation.

Short-term exposure weakened the effect of total long-term exposure by a small degree when both exposure variables were forced in full models, for example ß(PARINT) = 0.0180; p = 0.062 when including SPARACE, compared to ß(PARINT) = 0.0194; p = 0.019 when excluding SPARACE. In these models total long-term exposure was selected in stepwise procedures and the model with the lowest C^p. Short-term exposure was however, not significant when included as the only exposure variable in the model (SPARACE in table 4.9) and because of the fact that the effect of long-term exposure remained after subtracting the short-term component (PARACE2, PARINT2 in table 4.9), long-term exposure can be considered to have an effect which is independent of short-term exposure.

Appendix 5.8 (tables 1 and 2) gives a full summary of these results.

A distinction could not be made between herbicide exposure and paraquat specific exposure. Both variables were not included in the regression model due to high collinearity ($r = 0.99$).

Table 4.9 Summary of linear regression associations of exercise oximetry with exposure variables.

Predictor	ß	SE(ß)	P-value	Partial R^2	Model R^2
PARACE	0.00114	0.00056	0.0464	0.0474	0.106
PARINT	0.01941	0.00812	0.0190	0.0652	0.122
SPARACE	0.01198	0.00826	0.1506	0.0250	0.084
HERBACE	0.00116	0.00056	0.0391	0.0508	0.109
HERBINT	0.01938	0.00810	0.0192	0.0650	0.123
PARACE2	0.00126	0.00058	0.0504	0.0458	0.104
PARINT2	0.01984	0.00849	0.0219	0.0624	0.120

a) Total lifetime average intensity of paraquat (PARINT) or herbicide (HERBINT) exposure as well as cumulative paraquat (PARACE) and herbicide (HERBACE) exposure are significant predictors ($p < 0.05$)
b) Pure long-term measures (PARACE2, PARINT2) are also strongly associated.
c) SPARACE is not a significant predictor ($p = 0.1506$).
d) Average intensity was the strongest predictor.

Odds ratios are shown in table 4.10 for multiple logistic regression analysis of a dichotomous oximetry outcome based on different desaturation cutpoints.

Odds ratios are also shown in table 4.11 for multiple logistic regression analyses of a dichotomous oximetry outcome and dichotomous long-term exposure indices based on different cutpoints.

Alcohol consumption did not modify the effect of paraquat.

The prevalence of skin burns due to paraquat use was not significantly related to exercise oxygen desaturation (t-test, Fisher's Exact test and Logistic Regression) nor did it modify the effect of paraquat.

Reported asthma and tuberculosis prevalences did not have an effect on exposure-outcome relationships. There were no obvious differences between those with earlobe versus finger oximetry.

Table 4.10 The effect of changing cutpoints for dichotomised exercise desaturation in relation to dichotomised total lifetime cumulative paraquat exposure.

Desaturation cutpoint	Odds Ratio	95% CI
≥ 2%	2.09	0.49 - 8.92
≥ 3%	2.79	0.75 - 10.31
≥ 4%	5.66	1.39 - 23.06
≥ 5%	4.76	0.94 - 24.16

The cut-off level for exposure was 516 JEM days (75th percentile for the exposed group). The strength of the relationship tends to increase as the cutpoint for desaturation is increased.

Table 4.11 The effect of changing cutpoints for dichotomised total lifetime cumulative paraquat exposure in relation to dichotomised exercise desaturation.

Exposure cutpoint	Odds Ratio	95% CI
≥ 250 JEM* days	1.09	0.97 - 1.21
≥ 700 JEM* days	2.72	1.85 - 7.44

The cut-off level for desaturation was ≥ 3%. The strength of the relationship tends to increase as the cutpoint for exposure is increased.

* JEM = Job Exposure Matrix (see methods)

4.3.5 Relationship between lung function and oximetry

Exercise desaturation was not significantly associated with lung function including diffusion capacity even after adjusting for long-term exposure, age , height, weight, smoking and alcohol.

4.4 References

1. European Community for Coal and Steel mine. Bulletin European de Physiolopathogie Respiratoire 1983; 19 Suppl 5: 7-95.

CHAPTER 5 DISCUSSION

5.1 The basic finding

This study is the first to examine the patho-physiological effect of long term low dose paraquat exposure on exercise oximetry. The main finding is a small but significant effect. This is indicated by the fact that the effect was found consistently despite the use of different exposure indices and different modelling techniques. The effect of long-term paraquat exposure is significant even when accounting for short-term exposure. This suggests that exercise oximetry is a sensitive test for the patho-physiological effect expected and seems suitable for the early detection of respiratory illhealth due to paraquat exposure and possibly exposure to other fibrogenic agents.

5.2 Biological mechanism

The primary biochemical mechanism of acute paraquat toxicity (chapter 1) and the effect of pulmonary fibrosis on lung function (chapter 2) have been described in the first two chapters. Briefly, the cell toxicity of paraquat has been linked to its redox reaction with oxygen and reducing equivalents which initiate a number of proposed toxic reactions inside the cell. Cell death, tissue inflammation and eventually pulmonary fibrosis results. Fibrosis causes a decrease in inspiratory capacity due to a stiffening of the lungs. This reduces ventilatory capacity leading to a decrease in ventilatory-perfusion ratios which could

result in hypoxemia, especially during exercise.

Damage of the alveolar capillary membrane could also cause diffusion limitations between alveoli and blood. This could result in hypoxemia during exercise when oxygen diffusion has to occur rapidly because of increased blood flow.

As mentioned in chapter one, previously reported total (respiratory and skin) paraquat exposures of 12-170 mg/kg body-weight/hour of knapsack sprayers are higher than paraquat doses which cause chronic injury in animals. Long-term low dose paraquat exposure in agrochemical applicators and mixers could result in lung injury, especially in cases where absorption is increased by skin damage.

5.3 Validity of exercise oximetry

The validity of exercise oximetry as a method for measuring oxygen saturation and as a respiratory health measurement has been discussed in chapter 2. Briefly, oximetry has been shown to correlate with invasive measurements and has been shown to be a more sensitive predictor of respiratory disorders than subjective clinical assessment, spirometry, diffusion capacity and radiography.

5.4 Clinical significance of the basic finding

The regression coefficient of total cumulative exposure (PARACE)

in table 4.9 projects that 12.5 JEM years of cumulative paraquat exposure (equivalent to mixing paraquat every day for 12.5 years) will produce 5% exercise oxygen desaturation, commonly regarded as clinically significant (1). None of the subjects that performed a successful exercise test, had that level of lifetime cumulative paraquat exposure suggesting that exposures in the study sample were too low to produce clinically significant desaturation. This perhaps explains the absence of clinical and subclinical effects on lung function testing. One should be careful, however, in drawing conclusions beyond the range of the data. If the median lifetime average intensity of paraquat exposure (13 JEM days) and the median short-term paraquat exposure (45 JEM days) in the study sample are used to indicate the amount of JEM-days that on average could be accumulated in one calender year, then 12.5 JEM years translate to a lifetime of paraquat exposure. However, exposures in the study sample seemed to be low.

Table 5.1 shows that the prevalence of clinically significant desaturation increased in a dose-dependent manner with increasing paraquat exposure and that the relative prevalence of the highest exposure category compared to the lowest exposure category was 2.85 while the difference in the mean desaturation was 1.54%.

Table 5.1 The effect of different levels of total cumulative paraquat exposure on exercise oxygen desaturation

Exposure category (days)	n	Prevalence of desat.	Mean desaturation (%)
0	37	10.81	2.08
> 0 and ≤ 200	27	22.22	2.37
> 200 and ≤ 516	13	23.08	3.15
> 516	13	30.77	3.62

Note: Desaturation > 4%

5.5 Previous studies

Guitterez et al. (personal communication with C Hogstedt) found a positive relationship between paraquat exposure and reported dyspnea on walking and episodic wheezing accompanied by shortness of breath in Nicaraguan workers. In that study the exposure group was divided into a low exposure group which did not report symptoms of paraquat exposure, and a high exposure group which reported symptoms. Two years of cumulative paraquat exposure was the cut-off level for the exposure groups. The level of exposure in our study is lower when considering that the average exposure in our study (190 JEM days amongst exposed) is lower than the lowest value (2 yrs = 730 days) in the Nicaraguan study. The fact that exposure in the Nicaraguan study was not measured using a JEM does not explain the differences in exposures in the two studies. Reported skin burns due to paraquat usage were also substantially higher in the Nicaraguan study. Long term paraquat use is known to cause skin damage. Low exposures and therefore low prevalences of skin burns could account for the lack of association to respiratory symptoms found in this study.

The presence of symptoms of long-term paraquat usage could be used to identify high exposure groups locally as in the Nicaraguan study. The low prevalence of skin burns precluded its incorporation into exposure calculations and weakened its use as a separate exposure variable and potential effect modifier in this study. Nevertheless, the average oxygen desaturation of the subjects who reported skin burns due to paraquat and who had

interpretable saturation traces (3) was high (4.67 %).

Previous studies (3, 4) also found no effect of paraquat exposure on FEV1, FVC, FEV1/FVC and carbon monoxide transfer factor. Low exposures and a lack of sensitivity in detecting subtle respiratory defects might be factors explaining these results. Sample size calculations indicated that the sample size in this study requires substantially larger exposure effects for oximetry than for respiratory symptoms, spirometry and diffusion capacity measurements. These exposure effects as a percentage of the mean of the respective outcomes are:

FVC : 7% (0.27 ml)

K_{co} : 8% (0.34 kPa)

DIFFSAT: 93 % (1.1%)

The fact that despite this, an exposure effect was measured with oximetry, indicates that the measurement of exercise desaturation is a sensitive test for measuring respiratory health. The exposure effect on diffusion capacity was less than originally estimated.

5.6 Selection biases

Various selection biases which might have given rise to an underestimation of the paraquat effect include the low response from small farms which might have excluded some relatively highly exposed workers from the study sample and low exposures compared

to other studies. The Healthy Worker Effect (HWE) in this cross-sectional study is not thought to be significant because:

Firstly the nature of adverse effects being sought are subtle and often subclinical, and are unlikely to result in gross disability leading to job loss or to death, and therefore loss to the study population.

Secondly, farm workers in South Africa appear to have limited labour market mobility. Those who lose their jobs, tend to remain as farm workers but on other farms in less demanding jobs (5) and may have appeared in our study as currently non-exposed subjects with a history of past exposure. In our study 6 subjects selected as current non-applicators were former paraquat spraymen.

Another variant of the Healthy Worker Effect, selection of healthy individuals into the farm worker workforce, is also likely to be very limited in the South African agricultural setting, given the lack of alternative employment opportunities, the low levels of unemployment in rural areas relative to urban areas (6) and the low-skill requirements of agricultural labour.

5.7 Misclassification

The lack of a gold standard for past paraquat exposure, non-existent agronomic records and very low literacy levels of farmworkers necessitated the use of a Job Exposure Matrix(JEM)

as a best estimate of exposures. The JEM was shown to be reasonably valid and repeatable in a study focusing on organophosphate exposure (7), although formal validation by industrial hygiene studies of workers involved in the job activities used in the JEM, is still required. The inclusion of farming sector in the JEM might have refined exposure dose estimation, although pome fruit farming was found to be the predominant farming sector in the previous study (7). A small proportion of herbicide sprayers also sprayed insecticides in the same job. This means that the herbicide and paraquat exposure estimates contained a small amount of insecticide exposure. Any misclassification arising from this and the use of the JEM would most likely have been non-differential given the blinded nature of exposure estimation. This might be expected to have biased any measured effect towards the null, except in the case of extreme exposure scenarios (8).

Formal validation of the JEMs for the deciduous fruit setting is essential and this requires one or more field industrial hygiene studies of workers involved in the job activities used in the JEM to confirm or adjust the priori estimates.

5.8 Recall bias

Recall bias might have been operative for the reporting of respiratory symptoms, but there was probably insufficient understanding by subjects of the effects of paraquat to cause them to over report. Observers in the different aspects of the

study were blind to all other aspects with the exposure questionnaire being administered before recording respiratory outcomes.

It is additionally very difficult for the subject to knowingly interfere with exercise-desaturation relationships in such a way as to bias the exposure-desaturation association away from the null.

5.9 Generalisability

Generalisability of these results is limited by the exclusion of females and the fact that it applies only to farm workers from the study. An unknown number of women are being employed in work involving agrochemical spraying in South Africa. Additionally, the study sample was obtained from farms belonging to two large co-operatives which export fruit to international markets. The infrastructure and safety practices on these farms would in general be of a higher standard than on other farms in South Africa. London(7) found the use of personal protective equipment on these farms to be high which could mean that pesticide exposures in this study were probably on the low end of the spectrum. The study population is unlikely to differ substantially from agricultural worker populations in other less developed countries.

5.10 Validation of field oximetry

The average resting saturation of 98.3% compares well with laboratory measurements by Taylor (1). The lowest resting oxygen saturation level in the sample of 95% indicates that all starting values in the sample were in the plateau region of the sigmoidal oxygen-haemoglobin dissociation curve, above the recommended cut-off of 94%. The significant predictors of exercise performance in this study (age and weight were significant predictors of the maximum workload achieved during exercise) are consistent with those measured in the literature (9-10). This shows conclusively that exercise oximetry can be used in a field setting.

One limitation of oximetry in general is the high proportion (28.6%) of unusable traces. This is unavoidable as the technique is subject to movement artefact from jerky cycling movements due to subjects straining and flailing their heads. Lack of familiarity with the cycle or the type of ergometer might have caused this, but even people who are very familiar with cycle ergometry and who use more sophisticated cycle ergometers can cause artifacts when approaching their maximum. A Biox type oximeter has been found to have the highest correlation to invasively measured oxygen desaturation in a group of COPD patients of a group of oximeters currently available on the market (11). Measurements could have been improved if the procedures of the exercise test were demonstrated to subjects in groups. This was not focused upon during exercise testing in the current study because of time and logistic constraints. Group

demonstrations and technological advances to reduce noise due to movement artefact in oximeters could substantially reduce the number of uninterpretable traces during exercise oximetry.

The non-significance of smoking and age, which are known risk factors for respiratory disease, as predictors of exercise desaturation in the study must be explained. Smoking was also not a consistent predictor for other outcome measures in the study and this point is discussed later. Age has a greater effect on spirometry than on oximetry which is reliant on the efficiency of gas exchange within the lungs and this is far more dependent upon regional inequalities of ventilation and perfusion due to lung disease. This is the first study that has used exercise oximetry in a field setting and more multivariate studies are required to explore the effect of age on exercise desaturation.

The amount of desaturation did not consistently predict lung function (refer to multivariate results), but this could be expected because exercise oximetry is a more sensitive respiratory health measurement than lung function testing. Sue (12) found diffusion capacity to be an insensitive, but specific marker of respiratory disease. Diffusion capacity and other respiratory health measurements are probably not sensitive tests for the detection of the expected subclinical nature of respiratory defect due to long-term paraquat exposure in this study population.

The high prevalence of desaturation at all cut-off levels (refer to univariate results) indicates the high sensitivity of oximetry. The test is however not specific for paraquat.

5.11 Other findings in the study

An interesting finding was that body weight was an unexpected predictor of exercise desaturation and transfer factor. This association is expected for spirometry where body status is a known predictor (spirometry involves measurement of ventilatory capacity). This indicates that low weight as a marker of poor socio-economic status may predict poor respiratory health. Mean heights and weights of the study group were extremely low, indicating serious nutritional and growth retardation problems manifesting as low weight for age and stunting. This is consistent with the finding in the previous study (6) where low serum albumin predicted poorer neurobehavioral function (vibration sense) in a similar group.

Consistent with other studies on similar populations (13), the lung function values in this study (FVC, FEV1) were lower than ECCS reference values (14). In a review by White (13) on spirometric values of healthy populations of subsaharan ancestry (including 9690 men), considerable variation in standardised spirometric values of individual studies were found. The standardised (age = 38 yrs and height 171 cm) spirometric values for this study calculated using the methods in the review are:

FVC (l): 4.07 (3.85 - 4.29)

FEV1 (l): 2.83 (2.61 - 3.05).

These values are higher than values found in grain mill and control factory workers in Cape Town (15) and lower than textile (16), asbestos (17) and bank workers (18) measured in South Africa, although factors such as calender year, geographic region and altitude should be considered when comparing measurements from individual populations (13).

This finding and the fact that the FEV1/FVC ratio was significantly below ECCS reference values suggests mild airflow obstruction present in this population. Regression analysis suggest that this is not smoking or paraquat related. The defect might be explained by adverse socio-environmental (SE) factors present in the study population (19).

The prevalence of past history of asthma was low and that of tuberculosis high when compared to that found in textile workers in South Africa (16) with similar anthropometric measurements. The prevalence of past history of tuberculosis seemed to be similar or lower than that found in industrial settings in Cape Town (15, 20).

The significant effects of age, weight, and difference between post- and pre-exercise heart rate on exercise are not unexpected. Weight, as a proxy for body size, and age are known predictors of performance in exercise testing (exercise performance

prediction equations includes age and weight). Heart rate is known to increase with exercise intensity (9).

The inconsistent relationship between smoking and reported respiratory symptoms and lung function is consistent with earlier studies performed on industrial workers (15, 20) and might be due to the low level of smoking (average of 7.5 cigarette pack years) despite the high percentage of smokers. The low percentage of non-smokers (15.2%) in the study might not have provided sufficient information to investigate smoking as a predictor of respiratory health in this study. The 'healthy smoker ' effect (phenomenon where healthy individuals tend to take up smoking more than unhealthy individuals) might explain the inconsistent relationships to smoking. There is evidence (22) that this phenomenon is operative in smoking populations.

5.12 Bradford-Hill criteria

Most of the Bradford-Hill criteria used for demonstrating causality, applicable in this study are fullfilled. **Strength** (the effect of paraquat was significant on a group of workers not highly exposed), **dose** (the effect was shown using linear regression and table 5.1 shows dose dependent effect), **biological plausibility** (cell toxicity mechanism involving the production of superoxide radicals) and **experimental evidence** (animal studies have shown paraquat effects in low doses) exists. Although the cross-sectional study design does not demonstrate **time ordering**, paraquat exposure could be assumed to precede respiratory desease

because there are no known selection effects operative explaining the reverse. Only **consistency** has not been demonstrated because this is the first study which has shown a long term effect of paraquat. However, this study has used more sensitive methods for measuring exposure and outcome compared to previous studies. **Specificity** and **analogy** are not applicable. The evidence could thus be said to be reasonably **coherent**.

5.13 Recommendations

According to current pesticide legislation, paraquat has no chronic health effects and is regarded as being safe for use under normal application conditions. This study has however indicated that long term paraquat exposure under normal application conditions could result in respiratory abnormalities. This result should at least emphasise the need to increase farmers' and farm workers' awareness of the possible health hazards of paraquat by informing them of the chronic health effects in addition to the known acute effects. This could encourage the increased use of protective clothing and safer and reduced application of paraquat. The study has also emphasised the importance of early effective treatment of paraquat burns. The need for further studies performed prospectively and studies performed on women, who might be more highly exposed, is highlighted.

The practicability and usefulness of exercise oximetry as a sensitive test in a field setting holds promise for the

investigation and possibly the early detection and secondary prevention of occupational respiratory disease. Exercise oximetry could be used for screening (biological monitoring) workers.

5.14 Conclusions

Exercise oximetry appears to be a more sensitive measure for subclinical respiratory effects than clinical symptoms or lung function tests. This study demonstrated a clear relationship between long term paraquat exposure and exercise oximetry independently of recent acute effects of exposure or sequelae of past poisoning episodes. Subtle occupational respiratory effects due to other agents should be researched further using this technique.

5.15 References

1. Taylor M.B., Whitwam J.G. The current status of pulse oximetry. Anaesthesia 1986; 41: 943-9

2. Bernardini P; Paraquat and diquat: toxicological aspects and occupational hazards; Archives di Scienze del Lavoro. 1986; 331(2) : 117 - 123

3. Howard JK, Sabapathy NN, Whitehead PA. A study of the health of Malaysian plantation workers occupationally exposed to paraquat. British Journal of Industrial Medicine. 1981; 38: 110 - 116

4. Senanayake N, Gurunathan G, Hart TB, Amerisinghe P, Babapulle M, Ellapolla SB, Udupihille M, Basanayake V. An epidemiological study of the health of Sri Lankan tea plantation workers associated with long term exposure to paraquat. British Journal of Industrial Medicine 1993; 50: 257 -263

5. Waldman PL. Here you will remain: Adolescent experience on farms in the Western Cape [MA Thesis] Cape Town: Department of Anthropology, University of Cape Towns, 1993

6. Donaldson A, Roux A. Education, employment and income of black South Africans in 1985. Development South Africa 1994;

11(1) : 131 - 143

7. London L, An investigation into the neurological and neurobehavioural effects of long-term agrochemical exposure among deciduous fruit farm workers in the Western Cape, South Africa, 1994 [MD Thesis]. Cape Town: Department of Community Health. University of Cape Town, 1994

8. Dosemeci M, Wacholder S, Lubin JH. Does nondifferential misclassification of exposure always bias a true effect towards the null? American Journal of Epidemiology; 132(4): 746-748.

9. Jones NL, Campbell EJM . Clinical exercise testing. 2nd ed. Philadelphia: W.B Saunders, 1982.

10. Hansen JE, Sue DY, Wasserman K. Predicted values for clinical exercise testing. American Review of Repiratory Desease 1984; 129 Suppl: S49 -S55

11. Würtemberger G, Muller S, Matthys H, Sokolov I. Accuracy of nine commercially available pulse oximeters in monitoring patients with chronic respiratory insufficiency. Monaldi Arch Chest Dis 1994; 49(4): 348 - 353.

12. Sue D Y, Oren A, Hansen JE, Wasserman K. Diffusion capacity for carbon monoxide as a predictor of gas exchange during exercise. New England Journal of Medicine 1987; 316 : 1301 - 6

13. White NW, Hanley JH, Lalloo UG, Becklake MR. Review and analysis of variation between spirometric values reported in 29 studies of healthy African Adults. American Journal of Respiratory and Critical Care Medicine 1994; 150: 358 - 5

14. European Community for Coal and Steel. Bulletin European Physiolopathogie Respiratoire 1983; 19 Suppl 5: 7-95

15. Yach D. Myers J. Bradshaw D. Benatar SR. A respiratory epidemiologic survey of grain mill workers in Cape Town, South Africa. American Review of Repiratory Desease 1985; 131: 505-510

16. White N. Byssinosis in South Africa. A survey of 2411 textile workers. South African Medical Journal 1989; 75: 435-42.

17. Coetzee AM, Becker PJ. Lung function screening in industry. South African Medical Journal 1989; 67: 550 -3

18. Goldin JG. Spirometric and gas transfer measurements among normal adult South African men - an investigation into anthropometric, socio-economic, racial and environmental factors influencing lung function in Cape Town, South Africa [PhD Thesis]. Cape Town: Department of Community Health. University of Cape Town, 1994

19. Steinberg M, Becklake MR. Socio-environmental factors and lung function. South African Medical Journal 1986; 70: 270 - 4.

20. Myers JE. Cornell JE. Respiratory health of brickworkers in Cape Town, South Africa. Scandanavian Journal of Work and Environmental Health 1989; 15: 188-194.

21. Ragoucy-Sengler C, Pileire B, Daijardin JB. Survival from severe paraquat intoxication in heavy drinkers. Lancet 1991; 338: 1461.

22. Becklake MR, Lalloo U. 'The healthy smoker': a phenomenon of health selection? Respiration 1990; 57(3): 137-44.

APPENDICES

Appendix 1:
Questionnaires

Appendix 1.1 Questionnaire 1

STUDY NUMBER :
==========

GIFSTOFOPNAME - CERES / KOUEBOKKEVELD 1994

Department of Community Health

University of Cape Town

TOESTEMMING

Ons doen hierdie navorsingsstudie om vas te stel of die aard van u werk enige moontlike effekte op u gesondheid het. Hierdie informasie sal gebruik word om veiligheid in die werksituasie te verbeter.

Vrae sal gevra word, ondersoeke sal gedoen word en bloedtoetse sal geneem word om die studie moontlik te maak.

Enige-iets wat u aan ons vertel en alle resultate van die ondersoeke sal vertroulik hanteer word - dit beteken dat slegs u (en die verpleegster op die plaas) kennis sal dra van die resultate en niemand anders sonder u toestemming daarvan kennis sal kan neem nie.

'n Algemene rapport van die studie sal aan die plase verskaf word, maar individuele resultate sal nie daarin geïdentifiseer kan word nie. Ons sal u resultate aan u stuur, behalwe as u dit nie wil hê nie. Sal u so vriendelik wees om enige van die ondersoekers in kennis te stel indien u die resultate NIE wil hê nie.

Hiermee gee ek my toestemming om aan hierdie studie deel te neem:

..... (handtekening)

INHOUDSOPGAWE

A. INLEIDING

DATUM VAN ONDERHOUD:(dd/mm/jj) 1 5

NAAM VAN DIE ONDERHOUDVOERDER: 11 12

PLAASNAAM: 15

INLIGTING OOR DIE WERKER

1. Die werker se voornaam: 21

2. Die werker se van: 27 33

3. Werker se geboortedatum: (dd/mm/jj) 39

4. Die werker se Algemene Praktisyn (naam):.....

5. Wat is die hoogste standerd wat u voltooi het? 41

6. Vir hoeveel jaar was u op skool? 43

(Begin skoolgaan: ..... Opgehou: .....)

B. LEWENSGESKIEDENIS

1. Waar is u gebore?

44 Naam van die plek:.....

45 Naam van die distrik:.....

Hoe lank het u daar gewoon?.....

2. Waar het u daarna gewoon?

47 Naam van die plek:.....

48 Naam van die distrik:.....

Hoe lank het u daar gewoon?.....

3. Waar het u daarna gewoon?

50 Naam van die plek:.....

51 Naam van die distrik:.....

Hoe lank het u daar gewoon?.....

4. Waar het u daarna gewoon?

53 Naam van die plek:.....

54 Naam van die distrik:.....

Hoe lank het u daar gewoon?.....

5. Waar het u daarna gewoon?

56 Naam van die plek:.....

57 Naam van die distrik:.....

Hoe lank het u daar gewoon?.....

6. Waar het u daarna gewoon?

59 Naam van die plek:.....

60 Naam van die distrik:.....

Hoe lank het u daar gewoon?.....

7. Waar het u daarna gewoon?

62 Naam van die plek:.....

63 Naam van die distrik:.....

Hoe lank het u daar gewoon?.....

. Waar het u daarna gewoon?

Naam van die plek:..... 65

Naam van die distrik:.....

Hoe lank het u daar gewoon? 67

. Waar het u daarna gewoon?

Naam van die plek:..... 68

Naam van die distrik:.....

Hoe lank het u daar gewoon? 70

0. Waar het u daarna gewoon?

Naam van die plek:..... 71

Naam van die distrik:.....

Hoe lank het u daar gewoon? 73

TABEL 1: Vir elke woonplek bo, vul die tabel in. 1

Tipe plek (sleutel)	Duur	Losies (Ja/Nee)
1.....	.....	.....
2.....	.....	.....
3.....	.....	.....
4.....	.....	.....
5.....	.....	.....
6.....	.....	.....
7.....	.....	.....
8.....	.....	.....
9.....	.....	.....
10.....	.....	.....

5 9 13 17 21 25 29 33 37 41 45

SLEUTEL

1. stad
2. dorp
3. klein dorp
4. plaas
5. plaas en ander plek
6. klein dorp en ander plek
7. ander

EERSTE PLAAS

46 PLEKNOMMER: ..... PLEKNAAM: .....

1. Waarmee is daar geboer?

47 .....

49 .....

51

2. Waar was u huis geleë in verhouding met die naaste boord, wingerd of landery (posisie) SLEUTEL (*)

53 .....

SLEUTEL:

1.in die landery / boord / wingerd
2.langs die landery / boord / wingerd (< 10 m)
3.oorkant die pad / rivier

Identifiseer 'n landmerk en vergelyk die afstande met die afstande in die werker se situasie:

4.10 - 100 m vanaf die landery / boord / wingerd
5.100 - 1000 m vanaf die landery / boord / wingerd
6.>1000 m vanaf die landery / boord / wingerd

3. Is die boord, wingerd of landerye met gifstowwe gespuit? 1.JA 2.NEE 3.NIE SEKER

54

INDIEN JA:

Is die spuitwerk gedoen met behulp van 'n:

55 * Rugsak? 1.JA 2.NEE 3.NIE SEKER

56 * Trekker? 1.JA 2.NEE 3.NIE SEKER

57 * Vliegtuig? 1.JA 2.NEE 3.NIE SEKER

TWEEDE PLAAS

PLEKNOMMER: ..... PLEKNAAM: 58

1. Waarmee is daar geboer? 60

..... 62

..... 64

2. Waar was u huis geleë in verhouding met die naaste boord, wingerd of landery (posisie) SLEUTEL (*)

..... 65

3. Is die boord, wingerd of landerye met gifstowwe gespuit? 1.JA 2.NEE 3.NIE SEKER 66

INDIEN JA: Is die spuitwerk gedoen met behulp van 'n:

* Rugsak? 1.JA 2.NEE 3.NIE SEKER 67

* Trekker? 1.JA 2.NEE 3.NIE SEKER 68

* Vliegtuig? 1.JA 2.NEE 3.NIE SEKER 69

DERDE PLAAS

PLEKNOMMER: ..... PLEKNAAM: 70

1. Waarmee is daar geboer? 72

..... 74

..... 76

2. Waar was u huis geleë in verhouding met die naaste boord, wingerd of landery (posisie) SLEUTEL (*) 1 77

..... 5

3. Is die boord, wingerd of landerye met gifstowwe gespuit? 1.JA 2.NEE 3.NIE SEKER 6

INDIEN JA: Is die spuitwerk gedoen met behulp van 'n:

* Rugsak? 1.JA 2.NEE 3.NIE SEKER 7

* Trekker? 1.JA 2.NEE 3.NIE SEKER 8

* Vliegtuig? 1.JA 2.NEE 3.NIE SEKER 9

VIERDE PLAAS

10 PLEKNOMMER: ..... PLEKNAAM: .....

1. Waarmee is daar geboer?

11 .....

13 .....

15

2. Waar was u huis geleë in verhouding met die naaste boord, wingerd of landery (posisie) SLEUTEL (*)

17 .....

3. Is die boord, wingerd of landerye met gifstowwe gespuit? 1.JA 2.NEE 3.NIE SEKER

18

INDIEN JA: Is die spuitwerk gedoen met behulp van 'n:

19 * Rugsak? 1.JA 2.NEE 3.NIE SEKER

20 * Trekker? 1.JA 2.NEE 3.NIE SEKER

21 * Vliegtuig? 1.JA 2.NEE 3.NIE SEKER

VYFDE PLAAS

22 PLEKNOMMER: ..... PLEKNAAM: .....

1. Waarmee is daar geboer?

23 .....

25 .....

27

2. Waar was u huis geleë in verhouding met die naaste boord, wingerd of landery (posisie) SLEUTEL (*)

29 .....

3. Is die boord, wingerd of landerye met gifstowwe gespuit? 1.JA 2.NEE 3.NIE SEKER

30

INDIEN JA: Is die spuitwerk gedoen met behulp van 'n:

31 * Rugsak? 1.JA 2.NEE 3.NIE SEKER

32 * Trekker? 1.JA 2.NEE 3.NIE SEKER

33 * Vliegtuig? 1.JA 2.NEE 3.NIE SEKER

SESDE PLAAS

PLEKNOMMER: ..... PLEKNAAM: 34

1. Waarmee is daar geboer? 36

..... 38

..... 40

2. Waar was u huis geleë in verhouding met die naaste boord, wingerd of landery (posisie) SLEUTEL (*)

..... 41

3. Is die boord, wingerd of landerye met gifstowwe gespuit? 1.JA 2.NEE 3.NIE SEKER 42

INDIEN JA: Is die spuitwerk gedoen met behulp van 'n:

* Rugsak? 1.JA 2.NEE 3.NIE SEKER 43

* Trekker? 1.JA 2.NEE 3.NIE SEKER 44

* Vliegtuig? 1.JA 2.NEE 3.NIE SEKER 45

SEWENDE PLAAS

PLEKNOMMER: ..... PLEKNAAM: 46

1. Waarmee is daar geboer? 48

..... 50

..... 52

2. Waar was u huis geleë in verhouding met die naaste boord, wingerd of landery (posisie) SLEUTEL (*) 53

.....

3. Is die boord, wingerd of landerye met gifstowwe gespuit? 1.JA 2.NEE 3.NIE SEKER 54

INDIEN JA: Is die spuitwerk gedoen met behulp van 'n:

* Rugsak? 1.JA 2.NEE 3.NIE SEKER 55

* Trekker? 1.JA 2.NEE 3.NIE SEKER 56

* Vliegtuig? 1.JA 2.NEE 3.NIE SEKER 57

AGSTE PLAAS

58 PLEKNOMMER: ..... PLEKNAAM: .....

1. Waarmee is daar geboer?

59 .....

61 .....

63

2. Waar was u huis geleë in verhouding met die naaste boord, wingerd of landery (posisie) SLEUTEL (*)

65 .....

3. Is die boord, wingerd of landerye met gifstowwe gespuit? 1.JA 2.NEE 3.NIE SEKER

66

INDIEN JA:

Is die spuitwerk gedoen met behulp van 'n:

67 * Rugsak? 1.JA 2.NEE 3.NIE SEKER

68 * Trekker? 1.JA 2.NEE 3.NIE SEKER

69 * Vliegtuig? 1.JA 2.NEE 3.NIE SEKER

NEGENDE PLAAS

70 PLEKNOMMER: ..... PLEKNAAM: .....

1. Waarmee is daar geboer?

71 .....

73 .....

75

2. Waar was u huis geleë in verhouding met die naaste boord, wingerd of landery (posisie) SLEUTEL (*)

76 .....

77

3. Is die boord, wingerd of landerye met gifstowwe gespuit? 1.JA 2.NEE 3.NIE SEKER

1

INDIEN JA:

Is die spuitwerk gedoen met behulp van 'n:

6 * Rugsak? 1.JA 2.NEE 3.NIE SEKER

7 * Trekker? 1.JA 2.NEE 3.NIE SEKER

8 * Vliegtuig? 1.JA 2.NEE 3.NIE SEKER

TIENDE PLAAS

PLEKNOMMER: ..... PLEKNAAM: 9

1. Waarmee is daar geboer? 11

..... 13

..... 15

2. Waar was u huis geleë in verhouding met die naaste boord, wingerd of landery (posisie) SLEUTEL (*)

..... 16

3. Is die boord, wingerd of landerye met gifstowwe gespuit? 1.JA 2.NEE 3.NIE SEKER 17

INDIEN JA: Is die spuitwerk gedoen met behulp van 'n:

* Rugsak? 1.JA 2.NEE 3.NIE SEKER 18
* Trekker? 1.JA 2.NEE 3.NIE SEKER 19
* Vliegtuig? 1.JA 2.NEE 3.NIE SEKER 20

==========

11. Het u ooit SAAM MET IEMAND in die huis gewoon wat:

a) Vir 'n firma gewerk het waar gifstowwe vervaardig is? 1.JA 2.NEE 3.NIE SEKER 21

INDIEN JA, gee die aantal jare: 23

b) Vir iemand gewerk wat gifstowwe versprei het? 1.JA 2.NEE 3.NIE SEKER 24

INDIEN JA, gee die aantal jare: 26

c) Gifstowwe in geboue teen plae aangewend het? 1.JA 2.NEE 3.NIE SEKER 27

INDIEN JA, gee die aantal jare: 29

d) Gifstowwe gespuit het op 'n plaas 1.JA 2.NEE 3.NIE SEKER 30

INDIEN JA, gee die aantal jare en wie dit gedoen het: 32

.....

12. Het u ooit naby 'n fabriek wat gifstowwe vervaardig gewoon? 1.JA 2.NEE 3.NIE SEKER 33

INDIEN JA, gee die aantal jare: 35

C. WERKSONDERVINDING

1. EERSTE WERK

1. Wat was u eerste werk? (ook deeltydse werk terwyl op skool of terwyl woonagtig by ouers of seisoenwerk op 'n plaas):

.....

36 2. Hoe oud was u toe u begin werk het? .....

38 3. Watter soort werkplek was dit? .....

40 4. Beskryf die werk wat u gedoen het (wat het u die meeste van die tyd gedoen?):

.....

.....

43 5. Waar was hierdie werk? .....
(Pleknaam en distrik)

2. TWEEDE WERK

1. Watse werk het u daarna gedoen?

.....

44 2. Hoe oud was u toe u die werk begin het? .....

46 3. Watter soort werkplek was dit? .....

48 4. Beskryf die werk: (die meeste van die tyd gedoen?):

.....

.....

51 5. Waar was hierdie werk? .....
(Pleknaam en distrik)

3. DERDE WERK

1. Watse werk het u daarna gedoen?

.....

52 2. Hoe oud was u toe u die werk begin het? .....

54 3. Watter soort werkplek was dit? .....

6 4. Beskryf die werk: (die meeste van die tyd gedoen?):

.....

.....

54 5. Waar was hierdie werk? .....
(Pleknaam en distrik)

4. VIERDE WERK

1. Watse werk het u daarna gedoen?

.....

2. Hoe oud was u toe u die werk begin het? 61

3. Watter soort werkplek was dit? 63

4. Beskryf die werk: (die meeste van die tyd gedoen?): 66

.....

.....

5. Waar was hierdie werk? 67
(Pleknaam en distrik)

5. VYFDE WERK

1. Watse werk het u daarna gedoen?

.....

2. Hoe oud was u toe u die werk begin het? 69

3. Watter soort werkplek was dit? 71

4. Beskryf die werk: (die meeste van die tyd gedoen?): 74

.....

.....

5. Waar was hierdie werk? 75
(Pleknaam en distrik)

6. SESDE WERK 1 5

1. Watse werk het u daarna gedoen?

.....

2. Hoe oud was u toe u die werk begin het? 7

3. Watter soort werkplek was dit? 9

4. Beskryf die werk: (die meeste van die tyd gedoen?): 12

.....

.....

5. Waar was hierdie werk? 13
(Pleknaam en distrik)

7. **SEWENDE WERK**

1. Watse werk het u daarna gedoen?

.....

14 2. Hoe oud was u toe u begin werk het? .....

16 3. Watter soort werkplek was dit? .....

18 4. Beskryf die werk wat u gedoen het (wat het u die meeste van die tyd gedoen?):

.....

.....

21 5. Waar was hierdie werk? .....
(Pleknaam en distrik)

8. **AGSTE WERK**

1. Watse werk het u daarna gedoen?

.....

22 2. Hoe oud was u toe u die werk begin het? .....

24 3. Watter soort werkplek was dit? .....

26 4. Beskryf die werk: (die meeste van die tyd gedoen?):

.....

.....

29 5. Waar was hierdie werk? .....
(Pleknaam en distrik)

9. **NEGENDE WERK**

1. Watse werk het u daarna gedoen?

.....

30 2. Hoe oud was u toe u die werk begin het? .....

32 3. Watter soort werkplek was dit? .....

4 4. Beskryf die werk: (die meeste van die tyd gedoen?):

.....

.....

37 5. Waar was hierdie werk? .....
(Pleknaam en distrik)

10. TIENDE WERK

1. Watse werk het u daarna gedoen?

.....

2. Hoe oud was u toe u die werk begin het? 39

3. Watter soort werkplek was dit? 41

4. Beskryf die werk: (die meeste van die tyd gedoen?): 44

.....

.....

5. Waar was hierdie werk? 45
(Pleknaam en distrik)

TABEL 2:

Dui vervolgens aan in watter kategorie elk van die voorafgaande soorte werk val, deur dit A, B, C of D te noem, soos hieronder aangedui:

Landbou - A
Bosbou - B
Gifstofvervaardiging, Fabriek of Vervoer - C
Munisipaliteit - D

As dit ander werk is - O

Kategorie:	Jaar:	
WERK 1:	.....	48
WERK 2:	.....	51
WERK 3:	.....	54
WERK 4:	.....	57
WERK 5:	.....	60
WERK 6:	.....	63
WERK 7:	.....	66
WERK 8:	.....	69
WERK 9:	.....	72
WERK 10:.....	.....	75

vul nou asb. die ooreenstemmende seksies oor spesifieke bedrywighede in: LANDBOU, BOSBOU, FABRIEK EN VERVOER, MUNISIPALITEIT
*(word gevind in die ekstra leêrs wat voorsien is)

1

11. ANDER WERK

3

* Is daar enige ander werk wat u voorheen gedoen het, wat u nog nie genoem het nie, waarin u kontak gehad het met gifstowwe?

6 1.JA 2.NEE 3.NIE SEKER

INDIEN JA:

.1 Watter soort werkplek was dit? .....

7

.2 Beskryf die werk: (wat het u die meeste van die tyd gedoen?):

9 .....

.....

12 .3 Waar was hierdie werk? (Dorp of distrik) .....

.4 Vir hoe lank het u die werk gedoen?

13 Jare: ..... Maande: .....

(Hoe oud was u toe u hierdie werk begin doen het en hoe oud was u toe u met die werk opgehou het)

As die werk een van die volgende bedrywighede is:

LANDBOU, BOSBOU, FABRIEK EN VERVOER, MUNISIPALITEIT

Vul dan die ooreestemmende seksies in (word gevind in die ekstra leêrs wat voorsien is)

12. CHECK VRAAG

1. Het u ooit vir iemand gewerk:

15 * wat gifstowwe versprei het 1.JA 2.NEE

16 * wat geboue binne en buite teen pes gespuit het 1.JA 2.NEE

17 * waar u betrokke was by die aflewering van plaagdoder 1.JA 2.NEE

As die werker ja op enige van bogenoemde vrae beantwoord het:

➡ VOLTOOI SEKSIE E

[MAAR as die werker REEDS die WERK GENOEM HET, ignoreer die vraag en gaan na die volgende vraag 13]

13. BESKERMINGMONDERING

1. Het u beskermingsmondering gekry as u gifstowwe hanteer het? 1.JA 2.NEE 18

2. Watse beskermingsmondering het u gekry as u gifstowwe hanteer het?

	VRYLIK:	SPOOR AAN:	WAARVOOR?	
1. Handskoene				21
2. Masker Tipe:				25
3. Oorpak				28
4. Plastiek				31
5. Ander Tipe:				35

3. Hoe gereeld het u die ..... gedra?

	1.ALTYD	2.MEESTE VAN DIE TYD	3.SOMS	4.NOOIT	
Handskoene					36
Masker					37
Oorpak					38
Plastiek					39
Ander					40

4. As u teen die einde van die dag klaargemaak het, wanneer het u die oorpak uitgetrek?

1. by die werk, voordat u huis toe is
2. nadat u by die huis gekom het of
3. net voordat u gaan slaap het?
4. ander (spesifiseer) :

..... 41

5. Hoe gereeld het u die oorpak gewas of laat was?

1. elke dag
2. nie elke dag nie, maar meer as een keer per week
3. een keer per week
4. minder as een keer per week

42

6. Waar het u die oorpak gewas? 43

7. Is daar lopende water by u huis? 1.JA 2.NEE 44

14. **GIF BY DIE HUIS**

45 * Het u ooit gifstowwe huis toe geneem om daar te gebruik? (bv. in u eie groentetuin) 1.JA 2.NEE

INDIEN JA:

46 a. Waarvoor? .....

.....

48 b. Watter soort gif? .....

* Het u ooit leë gifstofhouers (kanne) huis toe geneem om te gebruik?

50 1.JA 2.NEE

51 **INDIEN JA,** waarvoor?

.....

.....

D. HOUDING TEENOOR VEILIGHEIDSMAATREëLS

1. Hoe belangrik dink u is dit om handskoene te dra as u kontak het met plaagdoder?

   1. Baie belangrik
   2. Belangrik
   3. Maak nie veel van 'n verskil nie
   4. Van geen belang nie

   [ ] 53

2. Hoe belangrik dink u is dit om 'n masker te dra as u kontak het met plaagdoder?

   1. Baie belangrik
   2. Belangrik
   3. Maak nie veel van 'n verskil nie
   4. Van geen belang nie

   [ ] 54

3. Hoe belangrik dink u is dit om 'n oorpak te dra as u kontak het met plaagdoder?

   1. Baie belangrik
   2. Belangrik
   3. Maak nie veel van 'n verskil nie
   4. Van geen belang nie

   [ ] 55

4. Na u mening, wat is die gevaar wanneer u met gifstowwe werk?

   [ ][ ] 57

   .....

5. Op watter manier kan 'n mens vergiftiging voorkom?

   [ ][ ] 59

   .....

6. Dink u dat die manier waarop ander werkers met gifstowwe werk: (omkring die een wat gekies word)

   1.veiliger is as u manier

   2.dieselfde is as u manier [ ] 60

   3.nie so veilig is soos u manier nie

   4.kan nie duidelik antwoord gee nie

7. Kan 'n mens altyd beskermingsklere maklik gebruik?

   Verduidelik verder : ..... [ ][ ] 62

   .....

E. AKUTE BLOOTSTELLINGSGESKIEDENIS

1. Wanneer laas het u kontak gehad met plaagdoder, in die vorm van spuitwerk, meng of algemene hantering? (die datum of hoeveelheid weke gelede)

   .....

2. Wanneer het u plaagdoder begin spuit, meng of hanteer hierdie seisoen?

   .....

3. Gedurende die seisoen, hoe dikwels het u elke maand gespuit. Begin met die eerste maand van hierdie spuitseisoen:

TABEL 4:		
Maand:	Hoeveel weke per maand:	Hoeveel dae per week:
Januarie		
Februarie		
Maart		
April		
Mei		
Junie		
Julie		
Augustus		
September		
Oktober		
November		
Desember		
Januarie 1993		
Februarie		
Maart		

F. HUISHOUDELIKE BLOOTSTELLING

1. Gebruik u enige plaagdoder in u tuin of by die huis? 1.JA 2.NEE 51

INDIEN JA:

1 Hoe lank gebruik u dit reeds? 54

Jare.....Maande..... 56

2 Wanneer laas het u dit gebruik? 60
*Laaste datum

3 Hoe gereeld het u plaagdoder gebruik in die afgelope 3 maande? 62
*Hoeveelheid kere

4 Wanneer laas het u plaagdoder gekoop? 64
*Laaste datum 66

5 Wat is die naam van die plaagdoder? 68

.....

6 Is u in die verlede blootgestel aan plaagdoder by die huis? 69

1.Gereeld 3.Amper nooit
2.Soms 4.Nooit

2. Het u 'n stokperdjie wat vereis dat u daagliks gom gebruik vir meer as 'n maand op 'n slag? 1.JA 2.NEE 70

3. Gebruik u enige middels wat hout langer behoue laat bly? (preserveermiddels) 1.JA 2.NEE 71

INDIEN JA:

1 Hoe gereeld gebruik u die preserveermiddels? 72

1.Gereeld 2.Soms 3.Amper nooit 4.Nooit

2 Noem die preserveermiddel wat u die meeste gebruik: 74

.....

3 Vir hoeveel jaar gebruik u die preserveermiddel al? 76

Jare ..... Maande 78

4 Is u voorheen blootgestel aan houtpreserveermiddels by die huis? 79

1.Gereeld 3.Amper nooit
2.Soms 4.Nooit

1

3

6

7

4. Is daar enige iemand by die huis wat met plaagdoder werk? 1.JA 2.NEE 3.NIE SEKER

INDIEN JA:

1 Hoeveel mense by die huis werk met plaagdoder?

.....

2 Ten opsigte van elke persoon, die volgende :

4

12

15

PERSOON 1:

a.Waar werk die persoon? .....

b.Watse werk doen hy/sy? .....

c.Word die oorpak gewas voordat hy/sy huis toe kom elke dag? 1.JA 2.NEE 3.NIE SEKER

16

19

22

PERSOON 2:

a.Waar werk die persoon? .....

b.Watse werk doen hy/sy? .....

c.Word die oorpak gewas voordat hy/sy huis toe kom elke dag? 1.JA 2.NEE 3.NIE SEKER

23

26

29

PERSOON 3:

a.Waar werk die persoon? .....

b.Watse werk doen hy/sy? .....

c.Word die oorpak gewas voordat hy/sy huis toe kom elke dag? 1.JA 2.NEE 3.NIE SEKER

30

* Was u ooit aan gifstowwe blootgestel buite u werk? 1.JA 2.NEE 3.NIE SEKER

31

INDIEN JA,

* Was dit: 1.Gereeld 2.Somtyds 3.Amper nooit

32

* Vir hoe lank was u daaraan blootgestel?

.....jare en/of .....maande

G. NEUROLOGIESE SIMPTOME:

In die afgelope twee weke, het u enige van die volgende simptome gehad:

* MAAGPYN	1.JA 2.NEE	34
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	35
* GEVOEL DAT U WIL OPGOOI	1.JA 2.NEE	36
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	37
* LIGHOOFDIGHEID	1.JA 2.NEE	38
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	39
* MOEILIK GEVIND OM TE LOOP	1.JA 2.NEE	40
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	41
* GEVOELLOOSHEID IN HANDE OF VOETE	1.JA 2.NEE	42
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	43
* PRIKKELSENSASIE IN HANDE OF VOETE	1.JA 2.NEE	44
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	45
* OORPYN	1.JA 2.NEE	46
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	47
* TAMHEID IN ARMS EN BENE	1.JA 2.NEE	48
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	49
* PYN IN ARMS EN BENE	1.JA 2.NEE	50
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	51
* LOOPNEUS	1.JA 2.NEE	52
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	53
* KOPSEER	1.JA 2.NEE	54
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	55
* LOMERIGHEID	1.JA 2.NEE	56
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	57
* SWAAR GEVOEL OP U BORS	1.JA 2.NEE	58
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	59
* MOEGHEID	1.JA 2.NEE	60
Indien wel, het dit vir meer as drie maande aangehou?	1.JA 2.NEE	61

1 3

H. GESKIEDENIS VAN ROOKGEWOONTES

1. Rook u tans?

1 JA (gaan na 3.) 2 NEE (gaan na 2.)

2. Het u al ooit voorheen gerook?

1 JA (gaan na 3.) 2 NEE (STOP hier)

6 7 8 3. Hoe oud was u toe u begin rook het? ..... jaar

10 4. Wat rook u / het u gerook?

1. Sigarette
2. Pyp
3. Albei

5. Hoeveel rook u / het u gerook?

11 12

- Sigarette per dag:
1. Minder as 10 2. 10 tot 19 3. 20 tot 29 4. 30 en meer 5. Ander:.....

- Pyptabak per week:
1. Klein pakkie 2. Medium pakkie 3. Groot pak 4. Ander:

INDIEN TANS 'N ROKER:

13 6. Het u in die verlede meer of minder as nou gerook?

1 JA (gaan na .1) 2 NEE (gaan na 8.)

.1 Hoeveel het u altyd gerook?

14 - Sigarette per dag:
1. Minder as 10
2. 10 tot 19
3. 20 tot 29
4. 30 en meer
5. Ander: .....

- Pyptabak per week:
(wys verskillende groottes pakkies: groot, medium en klein)

15
1.Klein pakkie
2.Medium pakkie
3.Groot pakkie
4 Ander: .....

.2 Vir hoe lank (getal weke, maande of jare) het u soveel gerook?

16 18 .....

INDIEN 'N ROKER IN DIE VERLEDE:

7. Hoe oud was u toe u ophou rook het? 21

.....

8. Snuif of pruim u tabak? 22

1. Snuif
2. Pruim
3. Albei
4. Geen

9. Het u al ooit dagga probeer? 23

1 JA 2 NEE

INDIEN JA: INDIEN NEE: STOP hier

Rook u nou dagga? 24

1 JA 2 NEE

INDIEN JA: INDIEN NEE: STOP hier

a) Hoe gereeld rook u dagga? 25

1.elke dag
2.nie elke dag nie, maar meer as een keer per week
3.minder as een keer per week
4.partykeer, maar minder as een keer per maand
5.nooit

b) Het u ooit meer (of minder) as nou gerook? 26

1 JA 2 NEE

(STOP hier)

INDIEN JA:

* Hoe gereeld het u dagga gerook? 27

1.elke dag
2.minder as elke dag maar meer as een keer per week
3.minder as een keer per week
4.partykeer, maar minder as een keer per maand
5.nooit

* Vir hoe lank (weke, maande, jare) het u soveel dagga gerook? 29 31

.....

I. GESKIEDENIS VAN ALKOHOLGEBRUIK

1. Neem u tans alkohol?

1 JA (gaan na 3.)

2 NEE (gaan na 2.)

2. Het u voorheen alkohol geneem?

JA (gaan na 3.) NEE (stop hier)

3. Hoeveel drink u / het u gedurende die week gedrink?

	Bier	Wyn	"Harde hout"	Tuisgebrou
Maandag tot Donderdag	.....	.....	.....	.....
Vrydag	.....	.....	.....	.....
Saterdag	.....	.....	.....	.....
Sondag	.....	.....	.....	.....

SLEUTEL:

Bier dumpie: A
Bier quart: B
Bier "Pint": C
Bier blik: D
Bier lang blik:E
Brandewyn half jack: I
Brandewyn 750 ml: K
Wyn kan: F
Wyn bottel: G
Boks Wyn (5liter): H (kraantjie)
Boks Wyn (2 liter):HH
Brandewyn quarter jack: J
Brandewyn 1 liter: KK
Glase: L tot N
Beker: P

4. Hou oud was u toe u begin drink het? ..... jaar

5. INDIEN HY ALKOHOL SLEGS VOORHEEN GENEEM HET:

* Hoe oud was u toe u ophou drink het? ..... jaar
* Hoeveel jaar lank het u gedrink? ..... jaar
* Hoekom het u opgehou? .....

.....

6. **VIR BEIDE DIE WAT TANS ALKOHOL NEEM EN DIE WAT IN DIE VERLEDE ALKOHOL GENEEM HET**

* Wanneer u na 'n vriend toe gaan / gegaan het vir 'n drankie of as u na 'n kroeg toe gaan / gegaan het saam met vriende, hoeveel drankies drink u / het u gedrink? [ ][ ][ ] 50

.....

* Het u (al) ooit gevoel dat u minder moet drink? 1.JA 2.NEE [ ] 51

* Het mense u (al) ooit kwaad gemaak deur u drinkgewoontes te kritiseer? 1.JA 2.NEE [ ] 52

* Het u (al) ooit sleg of skuldig gevoel omdat u drink? 1.JA 2.NEE [ ] 53

* Het u (al) ooit vroeg in die oggend 'n drankie gedrink om u beter te laat voel of om oor u babelaas (hang over) te kom? 1.JA 2.NEE [ ] 54

* Dink u u drinkgewoontes is / was normaal? 1.JA 2.NEE 3.WEET NIE [ ] 55

* Het dit (al) ooit met u gebeur dat u wakkerword in die oggend nadat u die vorige aand gedrink het en nie kan onthou wat als die vorige aand gebeur het nie? 1.JA 2.NEE 3.NIE SEKER [ ] 56

* Kan / kon u maklik ophou drink na een of twee drankies? 1.JA 2.NEE 3.NIE SEKER [ ] 57

* Dink u vriende of familie / het u vriende of familie gedink dat u normale drinkgewoontes het / gehad het? 1.JA 2.NEE 3.NIE SEKER [ ] 58

* Was u (al) ooit in die hospitaal as gevolg van drank? 1.JA 2.NEE [ ] 59

* Het u (al) ooit vriende of 'n meisie verloor as gevolg van drank? 1.JA 2.NEE [ ] 60

* Het u (al) ooit u familie afgeskeep as gevolg van drank? 1.JA 2.NEE [ ] 61

* Het u (al) ooit u verantwoordelikhede (bv. by die werk) afgeskeep as gevolg van drank? 1.JA 2.NEE 3.NIE SEKER [ ] 62

homies ne!

* Het u (al) ooit, agv drank gehalusineer (skimbeelde gesien), of stemme gehoor wat agterna nie daar is / was nie en het u onbeheerbaar gebewe? 1.JA 2.NEE [ ] 63

* Het u (al) ooit na iemand toe gegaan (bv.'n dokter, verpleegster, 'n vriend of iemand by die werk) om u te help met u drinkgewoontes? 1.JA 2.NEE [ ] 64

65 * Het u (al) ooit in die moeilikheid gekom by die werk as gevolg van drank? 1.JA 2.NEE

66 * Wat dink u is normale drinkgewoontes?

68 (Getal drankies per dag) .....

70 * Wat dink u is abnormale drinkgewoontes? (d.w.s te veel)

72 (Getal drankies per dag) .....

7. **INDIEN HY TANS ALKOHOL NEEM:**

Het u ooit in die verlede meer (of minder) as nou gedrink?
1 JA (gaan na a) 2 NEE (gaan na 8)

6

a) Hoeveel het u gedurende hierdie periode gedrink?

	Bier	Wyn	"Harde hout"	Tuisgebrou
7 Maandag tot Donderdag	.....	.....	.....	.....
Vrydag	.....	.....	.....	.....
10 Saterdag	.....	.....	.....	.....
Sondag	.....	.....	.....	.....

13 * Vir hoe lank (weke, maande, jare) het u soveel gedrink?

15 .....

8. Gedurende die afgelope week, van verlede Woensdag af, het u drinkpatroon verskil van die gewone?

17 1.JA 2.NEE 3.NIE SEKER

INDIEN JA, beskryf:

	Bier	Wyn	"Harde hout"	Tuisgebrou
18 Maandag tot Donderdag	.....	.....	.....	.....
Vrydag	.....	.....	.....	.....
21 Saterdag	.....	.....	.....	.....
Sondag	.....	.....	.....	.....

Werker se naam: .....

Huidige Plaasnaam:.....

1 5

SUBSEKSIE A: LANDBOU

1. **Watter werk is nou ter sprake? (die eerste, tweede, derde,....., neende of tiende, soos bo genoem)** 7

.....

2. Waarmee is daar geboer op die plaas? (Begin met die belangrikste produkte) 9

..... 11

..... 13

.....

3. Het u permanent of net tydens die seisoen op die plaas gewerk?

..... 14

1) Hoe lank het u hierdie werk gedoen? .....
(Jare of maande) 16

Begin: ..... Ophou: 18

2) In die werk was daar vir u wyn gegee op die plaas? 19

1.Nooit
2.Soms
3.Elke dag

Werker se naam: .....

Huidige Plaasnaam:.....

1 5

SUBSEKSIE A: LANDBOU

1. Watter werk is nou ter sprake? (die eerste, tweede, derde,....., neende of tiende, soos bo genoem) 7

.....

2. Waarmee is daar geboer op die plaas? (Begin met die belangrikste produkte) 9

..... 11

..... 13

.....

3. Het u permanent of net tydens die seisoen op die plaas gewerk?

..... 14

1) Hoe lank het u hierdie werk gedoen? .....

(Jare of maande) 16

Begin: ..... Ophou: 18

2) In die werk was daar vir u wyn gegee op die plaas? 19

1.Nooit
2.Soms
3.Elke dag

4. Het u enige van die volgende take gedoen terwyl u hier gewerk het:

20 1 **TREKKER BESTUUR** 1.JA 2.NEE

INDIEN JA, het dit enige van die volgende behels:

21 .1 Gifstowwe met 'n spuitpomp gespuit? 1.JA 2.NEE

22 Indien Ja, was u die hoofspuitman? 1 JA 2 NEE

.2 Trekker bestuur terwyl ander werkers van agter op die trekker met handspuite gif gespuit het?

23 1.JA 2.NEE

24 .3 Gifstowwe buitekant afgemeet of gemeng? 1.JA 2.NEE

25 .4 Gifstowwe in 'n gebou afgemeet of gemeng? 1.JA 2.NEE

26 2 **GIFSTOWWE SELF AANGEWEND PER HANDSPUIT VAN AGTER OP 'N TREKKER** 1.JA 2.NEE

INDIEN JA, sluit dit enige van die volgende in:

27 .1 Meng of uitmeet van gif in 'n toe kamer? 1.JA 2.NEE

28 .2 Meng of uitmeet van gif buitekant? 1.JA 2.NEE

29 .3 Het u insekdoder of onkruiddoder of albei gespuit? 1.INSEKD 2.ONKRUIDD 3.ALBEI

As die werker nie kan onthou nie, vra dan:

30 A Het u die gif op die grond gespuit of op die plante?

SLEUTEL:
1.Op die plante: INSEKD
2.Op die grond: ONKRUIDD

31 3 **GIF GESPUIT MET BEHULP VAN 'N RUGSAK** 1.JA 2.NEE

INDIEN JA, het dit enige van die volgende behels:

32 .1 Meng of uitgooi en afmeet van gif in 'n toe kamer? 1.JA 2.NEE

35 .2 Meng of uitgooi en afmeet van gif buitekant? 1.JA 2.NEE

34 .3 Die spuit van insekdoders, onkruiddoders of albei? 1.INSEKD 2.ONKRUIDD 3.ALBEI

As die werker nie kan onthou nie, vra dan:

35 A Het u die gif op die grond gespuit of op die plante?

SLEUTEL:
1.Op die plante: INSEKD
2.Op die grond: ONKRUIDD

4 GIFSTOWWE GEMENG OF UITGEGOOI EN AFGEMEET (Anders as werk 1 tot 3) 1.JA 2.NEE 36

INDIEN JA:

.1 Het u dit ooit in 'n toe kamer gedoen? 1.JA 2.NEE 37
.2 Het u dit ooit buitekant gedoen? 1.JA 2.NEE 38

5 'N CHEMIESE MIDDEL - DORMEX - OP BOME OF IN WINGERDE EN LANDERYE AANGEWEND MET 'N VERFKWAS OF RUGSAK OF MET 'N HANDSPUIT? 1.JA 2.NEE 39

6 SLEGS GRAANBOERDERYE

AS MERKER GEDIEN HET VIR 'N VLIEGTUIG WAT DIE LANDERYE MET GIF SPUIT? 1.JA 2.NEE 40

7 AS WERKTUIGKUNDIGE GEWERK MET 'n SPUITPOMP TREKKER MET DIE VERANTWOORDELIKHEID OM DIT IN STAND TE HOU OF GEREEDSKAP SKOONGEMAAK WAT VIR SPUITWERK GEBRUIK IS. 41

1 JA 2 NEE

8 SLEGS VRUGTEBOERDERYE

.1 HET U OOIT VRUGTE UITGEDUN? 1.JA 2.NEE 42
.2 HET U OOIT AS MONITORPERSOON GEWERK? 1.JA 2.NEE 43

9 SLEGS WINGERDE

HET U ENIGE VAN DIE VOLGENDE GEDOEN:

.1 Onderhoudswerk in die seisoen? 1.JA 2.NEE 44
.2 Met die suier gewerk? 1.JA 2.NEE 45
.3 Lote vasgemaak aan rankrame? 1.JA 2.NEE 46
.4 Trosse geöes? 1.JA 2.NEE 47
.5 Druiwe uitgedun? 1.JA 2.NEE 48

10 IN DIE WINGERDE OF BOORDE GEWERK TERWYL DAAR GESPUIT IS? (anders as 8 en 9) 1.JA 2.NEE 49

11 TUINWERK IN DIE BOER SE TUIN GEDOEN? 1.JA 2.NEE 50

12 VEE GEDIP? 1.JA 2.NEE 51

13 HET U IN HIERDIE WERK ENIGE ANDER KONTAK MET GIFSTOWWE GEHAD? 1.JA 2.NEE 52

INDIEN JA, spesifiseer: 54

.....

.....

INDIEN ENIGE VAN VOORAFGAANDE JA IS, VUL VOLGENDE TABEL IN:

TABEL A:

Hoeveel jaar lank het u hierdie werk gedoen?

Noem die maande van die jaar:

Hoeveel dae per week?

Soort werk:	Jare:	Maande vd jaar:	Dae/week:
1. Spuit (trekker) *	.....	.....	.....
*	.....	.....	.....
2. Handspuit			
3. Rugsak *	.....	.....	.....
*	.....	.....	.....
4. Meng *	.....	.....	.....
*	.....	.....	.....
5. Dormex			

55
59
63
67
71
1
3
6
10
14

TABEL A: (vervolg) Hoeveel jaar lank het u hierdie werk gedoen? Hoelank het u dit in die jaar gedoen?			
Soort werk:	Jare:	Dae, weke of maande in die jaar:	
6. Landmerker			21
7. Instandhouding van gereedskap			25
8. Uitdun			29
9. Monitor			33
10. Wingerd instandhouding			37
11. Tuinwerk			41
12. Veedip			45
13. Ander			49

13. Beskermingsmondering

50 1. Het u beskermingsmondering gekry in die bogenoemde werk? 1.JA 2.NEE

2. Watse beskermingsmondering het u gekry as u gifstowwe hanteer het?

	VRYLIK:	SPOOR AAN:	WAARVOOR?
51 1. Handskoene			
54 2. Masker Tipe:			
58 3. Oorpak			
61 4. Plastiek			
64 5. Ander Tipe:			

VERGIFTIGING IN HIERDIE WERK

68 15. Het u ooit siek geword van die gifstowwe? 1.JA 2.NEE

INDIEN JA:

69 71 1.Beskryf die omstandighede en die oorsaak en gevolg:

.....

.....

73 2. Het u 'n dokter besoek? 1.JA 2.NEE

74 3. Is u in die hospitaal opgeneem? 1.JA 2.NEE

75 **INDIEN JA**, moes u daar oorbly? 1.JA 2.NEE

HOSPITAAL se naam: .....

76 4. Moes u uit die werk wegbly? 1.JA 2.NEE

D

Werker se naam: .....

Huidige Plaasnaam: .....

1993/94 BLOOTSTELLING AAN ONKRUIDDODERS:

[Note to the interviewer: Gaan die rekords na vandat die vorige vraelys ingevul is (vraag nommer E: Akute blootstellingsgeskiedenis- bladsy 18) en voeg die volgende informasie daarby:]

1. Wanneer het u laas kontak gehad met gifstowwe, in die vorm van spuitwerk, meng of algemene hantering? (datum of hoeveelheid maande, weke of seisoene gelede)

   .....

2. Weet u wat die naam van die gifstowwe was waarmee u gewerk het?

   Gramazone: 1. JA 2. NEE
   Paraquat: 1. JA 2. NEE
   Ander: .....

   .....

2. Het u gifstowwe gemeng, hanteer of op die grond gespuit gedurende die afgelope jaar?

   Gemeng: 1. JA 2. NEE
   Hanteer: 1. JA 2. NEE
   Op die grond gespuit: 1. JA 2. NEE

3. Hoe dikwels het u met onkruiddoders gewerk vanaf verlede jaar Meimaand tot nou toe? (hetsy meng, hantering of spuit op die grond):

Maand:	Hoeveel weke per maand:	Hoeveel dae per week:
Mei 1993		
Junie 1993		
Julie 1993		
Augustus 1993		
September 1993		
Oktober 1993		
November 1993		
Desember 1993		
Januarie 1994		
Februarie 1994		
Maart 1994		
April 1994		
Mei 1994		

SUBSEKSIE A: LANDBOU

Hierdie vrae verwys na die ..... **WERK** wat jy genoem het in die vorige opname. (*Werksondervinding - bladsy 10 - wit vraelys*)

[Note to the interviewer: Indien die werker "Ja" geantwoord het op vrae 1 tot 3 in die vorige (liggroen) vraelys, verwys daarna met die vraag: "Jy het ons laaste keer vertel dat jy gifstowwe aagewend het in hierdie werk, hetsy met 'n handspuit, rugsak of met 'n 'hose gun' agterop die trekker . . . "]

1. Was die gifstowwe op die grond gespuit of op teen die bome/vrugte?

A { Op die grond: 1. JA 2. NEE
Op die bome: 1. JA 2. NEE
Albei: 1. JA 2. NEE

2. Indien jy op die grond gespuit het, het jy enige brandwonde opgedoen op jou rug of hande as gevolg van die gifstof waarmee jy gewerk het?

B { Op die rug: 1. JA 2. NEE
Hande: 1. JA 2. NEE
Enige ander: .....

3. Indien jy op die grond gespuit het, weet jy wat die naam van die gifstowwe was wat jy gebruik het?

B { Paraquat Chloride, Gramozone : 1. JA 2. NEE
Paraquat : 1. JA 2. NEE
Preeglone : 1. JA 2. NEE
Ander: .....

.....

[*Note to interviewer: Verwys na Tabel A op volgende bladsy van die liggroen vraelys en herhaal die aantal jare, maande en dae wat voorheen ingevul was.*]

4. Gedurende die aantal jare wat jy hierdie werk gedoen het, hoeveel van die tyd het jy spandeer om met 'n handspuit/rugsak of 'n "hose gun" agterop die trekker gifstowwe op die grond te spuit?

Maande van die jaar of seisoen: .....

Jan	Feb	Mar	Apr	Mei	Junie	Julie	Aug	Sept	Okt	Nov	Des

Hoeveel dae per week: .....

Maan	Dins	Woens	Donder	Vrydag	Saterdag	Sondag

5. Wat was die meeste agtereenvolgende dae wat jy ooit onkruiddoder gespuit het?

..... dae

6. Hoeveel spanne wat daar wat onkruiddoder gespuit het?

..... spanne

FARM WORKERS' HEALTH SURVEY

IDENTIFIKASIE NOMMER : (IDNUM) <idnum> .....

Ondervraer se naam: _____

PLAASWERKER SE NAAM : _____

PLAASNAAM : _____

Hierdie vrae het meestal met die bors en longe te doen. Antwoord asseblief JA of NEE waar moontlik.

A. HOES

A1. Hoes jy nogal baie? (COUGHA1)<Y>
(Tel die kere wat jy hoes vanaf bv. jou eerste sigaret of wanneer jy die eerste keer buitekant toe gaan soggens - dit sluit keel skoonmaak of kug uit.) <N>

Indien antwoord NEE , gaan na die volgende bladsy.

A2. Hoes jy gewoonlik 4 tot 6 keer per dag, 4 dae of meer in die week? (COUGHA2)<Y>
<N>

A3. Hoes jy as jy soggens opstaan of wanneer jy in die oggend wakker word? (COUGHA3)<Y>
<N>

A4. Hoes jy nogal baie gedurende die res van die dag of snags ? (COUGHA4)<Y>
<N>

Indien **JA** op enige van die bogenoemde vrae, beantwoord Vrae A5 en A6.

Indien **NEE** op bogenoemde vrae, trek 'n kring om die **NEE** en gaan na die volgende bladsy.

A5. Hoes jy gewoonlik so baie (soos voorheen beskryf) die meeste van die tyd vir 3 maande aaneen of meer as dit deur die jaar? (COUGHA5)<Y>
<N>

A6. Hoeveel jaar lank het jy al hierdie hoes? (COUGHA6)##

_____j

B. SLYM

B1. Hoes jy gewoonlik slym uit jou bors op ? {PHLEGMB1}<Y>
<N>

> Antwoord **JA** as dit gebeur met jou eerste sigaret of wanneer jy opstaan of as jy die slym insluk.
> Antwoord **NEE** as dit uit jou neus kom.)

B2. Hoes jy gewoonlik slym op meer as twee keer per dag, 4 of meer dae per week? {PHLEGMB2}<Y>
<N>

B3. Hoes jy gewoonlik slym op wanneer jy opstaan of onmiddelik nadat jy wakker word in die oggend? {PHLEGMB3}<Y>
<N>

B4. Hoes jy gewoonlik slym op enige ander tyd gedurende die dag of snags? PHLEGMB4}<Y>
<N>

> Indien **JA** op enige van die bogenoemde vrae, antwoord B5.
>
> Indien **NEE** op al die bg., gaan na die volgende bladsy.

B5. Hoes jy slym op soos vantevore beskryf die meeste van die tyd vir 3 maande aaneen of meer as dit gedurende die jaar? {PHLEGMB5}<Y>
<N>

B6. Hoeveel jaar lank het jy al probleme met slym? (*Het jy die probleem met slym al van kindsbeen af of net in die laaste paar jaar?*) {PHLEGMB6}##
_____j

C. EPISODES VAN HOES EN SLYM

C1. Is daar tye van die jaar wanneer jy vir 3 weke of langer **meer hoes en meer probleme met slym** ondervind? (Vir persone wat gewoonlik hoes en/of slym het) (..... *byvoorbeeld sekere seisoene?*) {EPSDEC1}<Y>
<N>

> **Indien JA op C1, beantwoord die volgende:**

C2. Vir hoe lank het jy al ten minste een so 'n episode per jaar ? {EPSDEC2}##
_____j

D. HYG NA ASEM (FLUIT IN DIE BORS)

D1. Het jy die afgelope jaar enige fluit- of suisgeluid in u bors gehad? (WHEZD1) <Y> <N>

Indien JA, gebeur dit:

D1.1 Wanneer jy verkoue het ? (WHEZ1D1)<Y> <N>

D1.2 Somtyds wanneer jy nie verkoue het nie? (WHEZ2D1)<Y> <N>

D1.3 Die meeste dae of nagte ? (WHEZ3D1)<Y> <N>

Indien 'NEE' gaan na Vraag E ; Indien 'JA':

D1.4 Raak jy ooit kortasem wanneer jy hierdie suisgeluid ondervind ? (WHEZ4D1)<Y> <N>

D1.5 Het jy hierdie suis- of fluitgeluid ondervind wanneer jy nie verkoue gehad het nie? (WHEZ5D1)<Y> <N>

D1.6 Het jy in die afgelope jaar ooit wakker geword met 'n benoude gevoel in die bors? (WHEZ6D1)<Y> <N>

D1.7 Het jy in die afgelope jaar wakker geword en gevoel jy kan nie asem kry nie? (WHEZ7D1)<Y> <N>

D2. Hoeveel jaar lank kry jy dit al ? (WHEEZD2)##

___j

D3. Het jy al ooit 'n aanval van hyging of fluit in die bors gehad wat jou kortasem laat voel het? (WHEEZD3)<Y> <N>

Indien JA op D3, beantwoord die volgende :

D4. Hoe oud was jy toe jy dit die eerste keer gekry het? (WHEEZD4)##

_____j

D5. Het jy dit al twee keer of meer kere gekry ? (WHEEZD5)<Y> <N>

D6. Het jy al ooit behandeling of medisyne benodig vir hierdie aanval(le)? (WHEEZD6)<Y> <N>

E. KORTASEM

E1. As jy te sleg voel om te loop as gevolg van enige ander siekte behalwe hart- of longsiektes, beskryf asseblief die siekte.

Aard van ongeskiktheid ..... {BREATHE1}

.....

E2. Raak jy kortasem wanneer jy vinnig op 'n gelykte of teen 'n effense opdraend loop? {BRETHE2}<Y> <N>

E3. Moet jy stadiger stap as ander mense van jou ouderdom omdat jy kortasem is? {BRETHE3}<Y> <N>

E4. Moet jy ooit stilstaan om asem te skep wanneer jy teen jou eie pas op 'n gelykte stap? {BRETHE4}<Y> <N>

E5. Moet jy ooit stilstaan om asem te skep wanneer jy omtrent 100 meter (of na 'n paar minute) op 'n gelykte gestap het ? {BRETHE5}<Y> <N>

E6. Is jy te kortasem om uit te gaan of raak jy kortasem wanneer jy aan- en uittrek? {BRETHE6}<Y> <N>

F. BORSVERKOUES EN BORSSIEKTES

F1. Wanneer jy verkoue kry, kry jy dit gewoonlik in die bors? (gewoonlik beteken meer as die helfte van die tyd). {CHESTF1}<Y> <N>

F2. Het jy gedurende die laaste 3 jaar enige borssiektes opgedoen wat jou van die werk af gehou of in die huis of in die bed gehou het? {CHESTF2}<Y> <N>

Indien JA op F2, beantwoord die volgende:
Indien NEE, gaan na die volgende bladsy.

F3. Het jy slym op gehoes met enige van hierdie siektes ? {CHESTF3}<Y> <N>

F4. Hoeveel keer die afgelope 3 jaar het jy sulke borskwale gehad (met baie slym), wat 'n week of langer aangehou het ? {CHESTF4} ## _____ keer

G. SIEKTE GESKIEDENIS

G1. Het jy enige long probleme gehad voor jy 16 jaar oud was? {HISTG1}<Y> <N>

G2. Het jy al ooit enige van die volgende siektes gehad:

G2.1 Aanvalle van brongitis ? *(Wanneer die hoes soos 'n blaf klink)* {G2HIST1A}<Y> <N>

Indien JA op G2.1 :

A. Is dit deur 'n dokter bevestig? *(Het die dokter gesê dit is brongitis?)* {G2HIST1B}<Y> <N>

B. Hoe oud was jy toe jy dit vir die eerste keer gekry het? {G2HIST1C}## _____j

G2.2 Longonsteking (Pneumonie)? (insluitend brongopneumonie) {G2HIST2A}<Y> <N>

Indien JA op G2.2 :

A. Is dit deur 'n dokter bevestig? *(Het die dokter gesê dit is longontsteking?)* {G2HIST2B}<Y> <N>

B. Hoe oud was jy toe jy dit vir die eerste keer gekry het? {G2HIST2C}## _____j

G2.3 Het jy al ooit hooikoors gehad? {G2HIST3A}<Y> <N>

Indien JA op G2.3 :

A. Was jy by 'n dokter wat gesê het dit is hooikoors? {G2HIST3B}<Y> <N>

B. Op watter ouderdom het dit begin? {G2HIST3C}## _____j

G2.4 Het jy al ooit enige sinus probleme gehad? {G2HIST4A}<Y> <N>

Indien JA op G2.4 :

A. Is dit deur 'n dokter bevestig? {G2HIST4B}<Y> <N>

B. Op watter ouderdom het dit begin? {G2HIST4C}## _____j

G2.5 Longtuberkulose (T.B.)? {G2HIST5A}<Y> <N>

Indien JA op G2.5:

A. Is dit deur 'n dokter bevestig? {G2HIST5B}<Y> <N>

B. Op watter ouderdom het dit begin? {G2HIST5C}## _____j

C. Hoeveel maande lank het jy behandeling gekry by 'n hospitaal en/of kliniek? {G2HIST5D}## _____m

D. Is jy meer as een keer behandel vir tuberkulose ? {G2HIST5E}<Y> <N>

E. Ontvang jy steeds behandeling vir tuberkulose? {G2HIST5F}<Y> <N>

G2.6 Het jy al ooit asma gehad ? {HISTG3A}<Y> <N>

Indien JA :

A. Gebruik jy op die oomblik medisyne of behandeling (bv. 'n spuitpomp) vir asma? {HISTG3A}<Y> <N>

B. Kry jy nog steeds asma? {HISTG3B}<Y> <N>

Indien NEE, gaan na F, indien JA:

C. Het die dokter gesê dit is asma? {HISTG3C}<Y> <N>

D. Op watter ouderdom het dit begin ? {HISTG3D} ## ___j

E. Het jy gedurende die afgelope jaar 'n asma-aanval gehad ? {HISTG3E}<Y> <N>

F. Indien jy dit nie meer kry nie, op watter ouderdom het dit opgehou? {HISTG3F} ## _____j

G. Kry enige ander familielede tans asma of het enigiemand in jou familie al voorheen asma gekry? {HISTG3G}<Y> <N>

Spesifiseer asseblief:

1. moeder {HISTG3G1} <Y>
2. vader {HISTG3G2} <Y>
3. broers of susters {HISTG3G3} <Y>
4. kinders {HISTG3G4} <Y>
5. ander {HISTG3G5} <Y>

G3. Het jy al ooit :

A. Enige ander borskwaal gehad ?

Indien **JA** spesifiseer asseblief:

_____

_____ {HISTG4A}

B. Enige bors-operasies gehad ?

Indien **JA** spesifiseer asseblief:

_____ {HISTG4B}

_____

C. Enige borsbeserings opgedoen ?

Indien **JA** spesifiseer asseblief:

_____ {HISTG4C}

_____

D. Enige ander siektes ?

Indien **JA** spesifiseer asseblief:

_____

_____

_____

_____

_____ {HISTG4D}

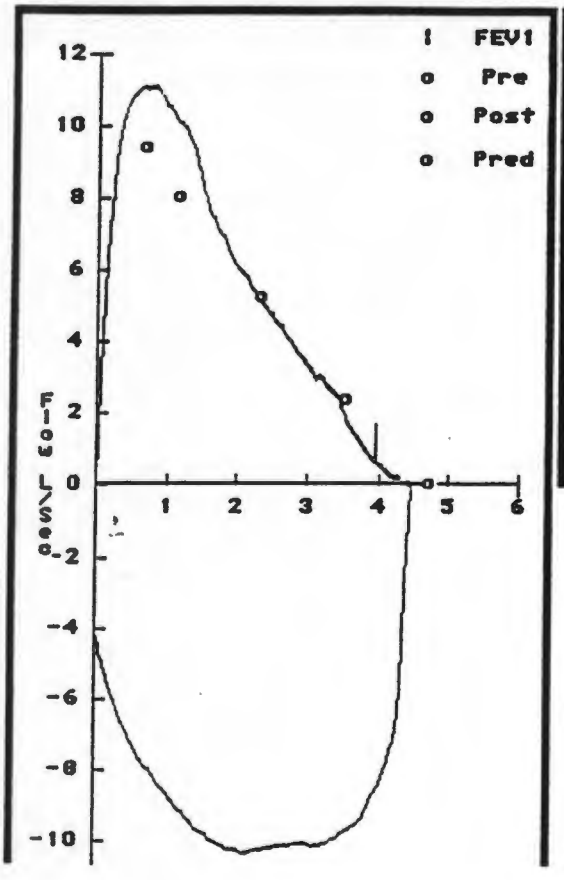
Appendix 2:

Lung Function Report Sheet

Cardiopulmonary Diagnostic Systems
350 Oak Grove Parkway, St. Paul MN 1-800-333-4137

Name: ID: P56 Date: 27-May-94
Race: Caucasian Height: 171 cm Weight: 85.0 kg Sex: M
Room: BSA: 1.97 Age: 30 yr
Dr. : DR WHITE Technician: MANDI

		PRE-BRONCH			POST-BRONCH		
		Actual	Pred.	%Pred.	Actual	%Pred.	%Chng
LUNG MECHANICS							
FVC	(L)	4.45	4.73	94			
FEV1	(L)	3.93	3.99	99			
FEV1/FVC	(%)	88	84				
MEF 25%	(L/sec)	10.17	8.00	127			
MEF 50%	(L/sec)	5.42	5.20	104			
MEF 75%	(L/sec)	2.63	2.34	112			
MEF MAX	(L/sec)	11.09	9.36	118			
MEF 25-75%	(L/sec)	4.94	4.73	105			
MEF 75-85%	(L/sec)	1.67					
FIVC	(L)	4.74					
FIF 50%	(L/sec)	10.34	5.50	188			
MEF 50%/FIF 50%		0.52	0.95				
LUNG DIFFUSION							
DLCOunc(ml/min/mmHg)		34.40	32.80	105			
DLVEOLAR VOLUME (L)		6.25	6.36	98			
DL/VA(ml/min/mmHg/L)		5.51	5.16	107			

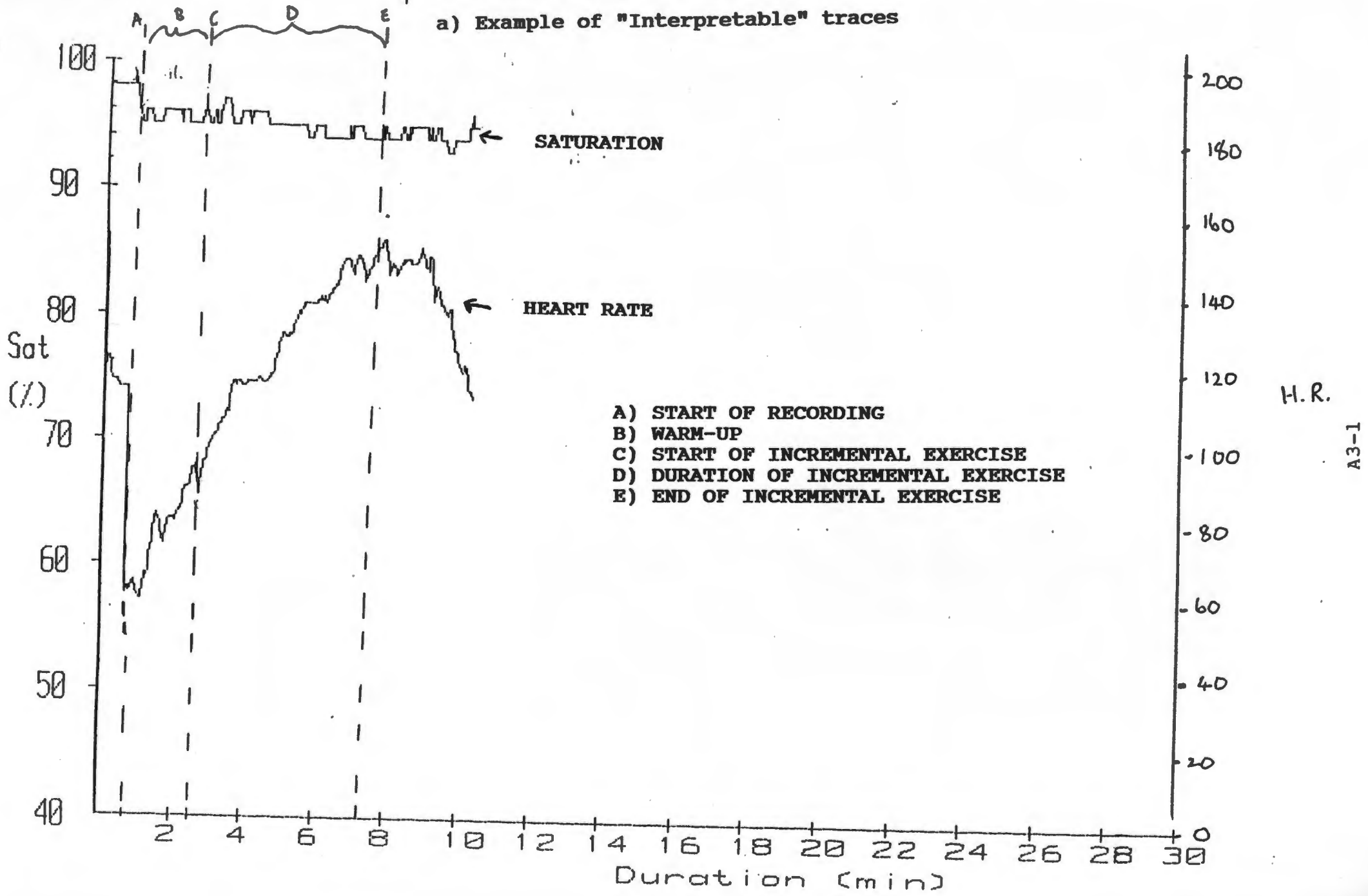


Appendix 3:

Examples of Saturation and Heart Traces recorded during exercise

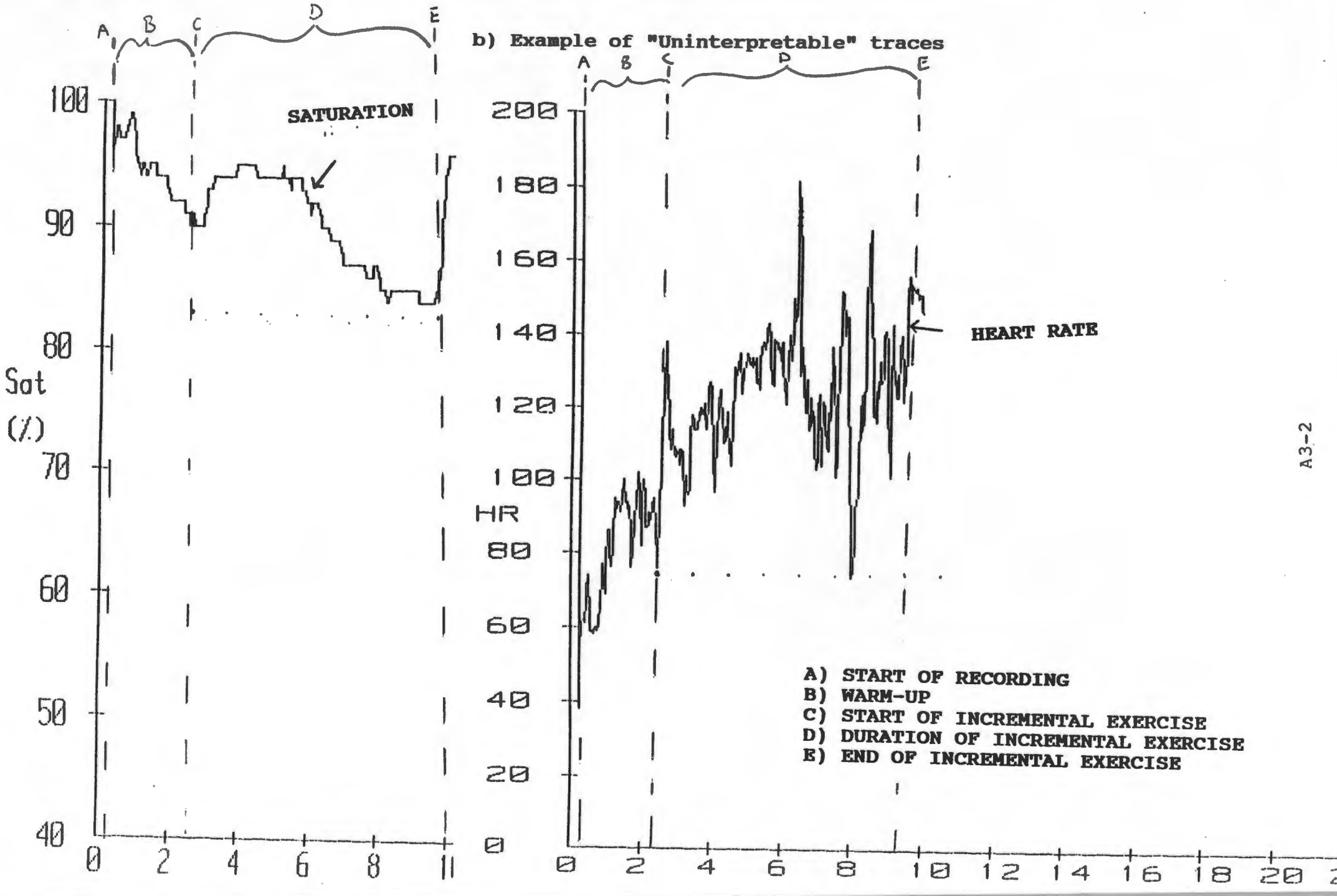
during exercise testing.

a) Example of "Interpretable" traces



A3-1

b) Example of "Uninterpretable" traces



Appendix 4:
Glossary of variables

APPENDIX 4 Glossary of variables

NOTE FOR ALL DICHOTOMOUS VARIABLES (DI) 1=YES; 2=NO UNLESS OTHERWISE SPECIFIED

Variable:	Definition:
General	
BMI	Body mass index (height/weight2)
BSA	Body surface area
HEIGHTCM	height (cm)
IDX	Study number
DATE	Survey date
NAME	Surname
NAME1	Name
SCHOOL	No of years attended school
WEIGHTKG	Weight (kg)
Respiratory Symptoms	
coughing:	
COUGHA1	Coughing (DI)
COUGHA2	Coughing > 4-6 per day; > 6 per wk (DI)
COUGHA3	Coughing in morning (DI)
COUGHA4	Coughing in rest of the day (DI)
COUGHA5	Coughing > 3 mnths (DI)
COUGHA6	no of yrs COUGHA5
COUGHA7	Coughing > 2 yrs (DI)
phlegm production:	
PHLEGMB1	Phlegm (DI)
PHLEGMB2	Phlegm > 4-6 per day; > 6 per wk (DI)
PHLEGMB3	Phlegm in morning (DI)
PHLEGMB4	Phlegm in rest of the day (DI)
PHLEGMB5	Phlegm > 3 mnths (DI)
PHLEGMB6	no of yrs PHLEGMB5
PHLEGMB7	Phlegm > 2 yrs (DI)
Episodes of coughing and slime:	
EPSDEC1	> 3 wks (DI)
EPSDEC2	no yrs of EPSDEC1
EPSDEC3	EPSDEC1 > 2 yrs (DI)
Wheezing:	
WHEZDI	Wheezing current year (DI)
WHEZ1D1	During cold (DI)
WHEZ2D1	Wheezing when no cold (DI)
WHEZ3D1	Most days and nights (DI)
WHEZ4D1	Shortness of breath when wheezing (DI)

WHEZ5D1	Wheezing when no cold (DI)
WHEZ6D1	Awoke with tight chest (DI)
WHEZ7D1	Awoke short of breath (DI)
WHEEZD2	No of yrs of wheezing
WHEEZD3	attack of wheezing and shortness of breath (DI)
WHEEZD4	age of first wheezing
WHEEZD5	> 2 WHEEZD3 (DI)
WHEEZD6	Treatment for wheezing (DI)
WHEEZD7	> 2 yrs wheezing (DI)

Shortness of breath (SOB):

BRETHE1	Description of SOB
BRETHE2	SOB during fast or incline walking (DI)
BRETHE3	> SOB than age-group (DI)
BRETHE4	SOB during normal walking (DI)
BRETHE5	SOB after 100m walking (DI)
BRETHE6	SOB normal activity (DI)

Chest Colds:

CHESTF	Cold in chest (DI)
CHESTF1	Chest cold during past 3 yrs + absent from work (DI)
CHESTF2	Slime production (DI)
CHESTF3	No of times in past 3 yrs

History of resp. illness:

HISTG1	Lung problems before 16 (DI)

(bronchitis)

G2HIST1A	bronchitis (DI)
G2HIST1B	medical confirmation (DI)

(pneumonia)

G2HIST2A	Pneumonia (DI)
G2HIST2B	medical confirmation (DI)

(hayfever)

G2HIST3A	Hayfever (DI)
G2HIST3B	medical confirmation (DI)

(sinus)

G2HIST4A	sinus (DI)
G2HIST4B	medical confirmation (DI)

(T.B)

G2HIST5A	TB (DI)
G2HIST5B	med confirm. (DI)
G2HIST5E	> 1 time TB treatment (DI)
G2HIST5F	Still TB treatment (DI)

(Asthma)

HISTG3A	past asthma (DI)
HISTG3AM	currently using med. for asthma (DI)
HISTG3B	still asthma (DI)
HISTG3C	med confirm. of asthma (DI)
HISTG3E	asthma during current yr.(DI)

(relatives with asthma)

HISTG3G1	mother (DI)
HISTG3G2	father (DI)
HISTG3G3	brothers or sisters (DI)
HISTG3G4	children (DI)
HISTG3G5	other relatives (DI)

HISTG3GN

(Other problems)

HISTG4A	Other chest problems
HISTG4B	chest operations (DI)
HISTG4C	chest injuries (DI)
HISTG4D	other illnesses (DI)

Respiratory tests

ALV	Alveolar volume (l)
ALV1	predicted ALV
ALV2	% predicted ALV
DLCOUN	CO transfer factor (ml/min/mmHg)
DLCOUN1	predicted DLCOUN
DLCOUN2	% predicted DLCOUN
DLVAMLM	CO transfer factor/ALV (ml/min/mmHg ?)
DLVAMLM1	predicted DLVAMLM
DLVAMLM2	% predicted DLVAMLM
FEFMAX	Maximum Forced expiratory (l/sec)
FEFMAX1	Predicted FEFMAX
FEFMAX2	% predicted FEFMAX
FEV1FVC	FEV1/FVC
FEV1FVC1	FEV1/FVC predicted
FEV1FVC2	FEV1/FVC % of predicted

FEV1L	FEV1 (l)

FEV1L1	predicted FEV1 (1)
FEV1L2	% predicted FEV1
FVCL	Forced vital capacity (1)
FVCL1	predicted FVC
FVCL2	% predicted FVC

Exercise:

continuous variables:

RESTHR	Resting pulserate (beats/min)
MAXHR	Maximum heart rate during exercise (beats/min)
HRPRED	Predicted maximum heart rate (beats/min)
DIFFHR	difference between MAXHR and RESTHR
RESTSAT	Resting saturation (%)
MAXSAT	Saturation at maximum exercise
DIFFSAT	difference between RESTSAT and MAXSAT
MAXWL	Maximum workload reached (kpm/min)
WLPRED	Predicted MAXWL
PERWLPRE	% of predicted MAXWL
VO2MAX	Maximum Oxygen consumption (1)
VO2MAXP	Predicted. VO2MAX
PERPREDV	% of predicted VO2MAX

Oximetry:
categorical variables:

TRACE3	DIFFSAT (DI); 1 ≥ 2%
TRACE4	DIFFSAT (DI); 1 ≥ 3%
TRACE5	DIFFSAT (DI); 1 ≥ 4%
TRACE6	DIFFSAT (DI); 1 ≥ 5%

Radiography:

continuous variable

PROF	Profusions (scale 0 - 10)

categorical variable

CPROF	PROF (DI); 1 ≥ score of 0
CPROF2	PROF (DI); 1 ≥ score of 1

EXPOSURE

continuous variables:

HERBACE	Total lifetime cumulative herbicide exposure
PARACE	Total lifetime cumulative paraquat exposure
SHERBACE	Short-term herbicide exposure
SPARACE	Short-term paraquat exposure
HERBINT	lifetime average intensity of herbicide

	exposure
PARINT	lifetime average intensity of paraquat exposure
PARACE2	PARACE - SPARACE
PARINT2	PARACE2/no of jobyears

categorical variables:

EXPA0	HERBACE (DI); 1 > 0
EXPA50	HERBACE (DI); 1 > 50 JEM days
EXPA100	HERBACE (DI); 1 > 100 JEM days
EXPA250	HERBACE (DI); 1 > 250 JEM days
EXPA700	HERBACE (DI); 1 > 700 JEM days
EXPP	short-term HERBACE (DI); 1 > 0 JEM days
EXPPA0	PARACE (DI); 1 > 0 JEM days
EXPPA50	PARACE (DI); 1 > 50 JEM days
EXPPA100	PARACE (DI); 1 > 100 JEM days
EXPPA250	PARACE (DI); 1 > 250 JEM days
EXPPA700	PARACE (DI); 1 > 700 JEM days
EXPINT13	PARINT (DI); 1 > 13 JEM days/yr
EXPINT34	PARINT (DI); 1 > 34 JEM days/yr
EXPS	SPARACE (DI); 1 > 0 JEM days
EXGRAD	Ordinal PARACE; 1 = JEM days, 2 > 0 and < 200 JEM days, 3 > 200 and < 516 JEM days, 4 > 516 JEM days
POISTOT2	previous history of paraquat poisoning (DI)

SMOKING AND ALCOHOL

continuous variables:

ALC	Alcohol consumption (kg)
NICX	20 cig. pack-years

categorical variables:

NICCAT	ALC (DI); 1 > 0
ETHCAT	ALC (DI); 1 > 0

Appendix 5:

Supplementary Results

Appendix 5 Supplementary Results
Appendix 5.1 Univariate results

TABLE 1 Continuous variables

Outcome (units)	Median	Mean	SD	n	Range
FVCL (l)		3.73	0.61	125	2.33 - 5.11
FVCL2 (l)		89.24	12.41	125	67 - 130
FEV1L (l)		3.06	0.57	125	1.38 - 4.39
FEV1L2 (l)		86.11	14.07	125	48 - 137
FEV1FVC	84	82.03	9.84	125	52 - 97
FEFMAX (l/sec)		7.73	1.91	125	2.68 - 12.04
FEFMAX2		89.23	21.2	125	35 - 138
DLCOUN (ml/min/kPa		4.10	0.75	107	2.28 - 5.65
DLCOUN2		106.40	18.96	107	69 - 177
ALV (l)		5.29	0.75	107	3.6 - 7.06
ALV2		91.48	11.10	107	67 - 123
DLVAMLM (ml/min/kPa/l		0.78	0.14	107	0.44 - 1.17
DLVAMLM2	114	117.12	22.35	107	70 - 209
MAXWL (Kpm/min)		1080.3	164.46	122	700 - 1500
PERWLPRE		103.45	19.80	122	59 - 170
RESTSAT	99	98.3	1.5	90	95 - 100
MAXSAT	96	95.8	2.7	90	86 - 100
DIFFSAT (%)	2	2.54	2.36	90	-1 - 10
RESTHR (beats/min)	65	68.8	15.2	122	60 - 120
MAXHR (beats/min)	170	168.7	12.2	122	137 - 200
DIFFHR	101.5	99.9	16.52	122	32 - 132
PERPREDH		89.6	6.65	122	73 - 104
VO2MAX (ml/min)		2357.9	335.6	122	1582 - 3210

Exposure (units)	Median	Mean	SD	n	Range
EYRTOT2 (yrs)	16.0	17.9	11.0	126	3.0 - 54.0
HERBACE (days)	154.4	436.9	763.2	76	1 - 5212
HERBINT (days/yr)	12.81	27.0	37.3	76	0.07 - 192.36
SHERBACE (days)	40	47.3	39.3	48	0.7 - 135
PARACE (days)	190.3	456.4	794.9	68	1.8 - 5196
PARINT (days/yr)	13.45	27.90	38.49	68	0.17 - 192.36
SPARACE (days)	45.0	51.6	40.2	41	0.7 - 135

Variables (units)	Median	Mean	SD	n	Range
WEIGHTKG (Kg)		56.1	8.9	125	35 - 85
BSA		1.6	0.14	125	1.22 - 1.97
HEIGHTCM (cm)		163.6	6.9	125	147 - 177
AGE (years)		34.2	9.9	126	18 - 65
ALC (Kg)	148.8			125	0 - 1298.7
NICX (packyears)	7.5	10.9	14.2	125	0 - 94.5

TABLE2 Categorical variables

Respiratory symptom:

Variable	n	Prevalence (%)
COUGHA1	126	57.1
COUGHA2	126	41.3
COUGHA3	126	43.7
COUGHA4	126	38.9
COUGHA5	126	11.9
COUGHA7	126	7.9
PHLEGMB1	126	32.5
PHLEGMB2	126	18.3
PHLEGMB3	126	23.8
PHLEGMB4	126	18.3
PHLEGMB5	126	10.3
PHLEGMB7	126	7.9
EPSDEC1	126	23.8
EPSDEC3	126	21.4
WHEZD1	126	46.8
WHEZ1D1	126	44.4
WHEZ2D1	126	15.1
WHEZ3D1	126	22.2
WHEZ4D1	126	25.4
WHEZ5D1	126	14.3
WHEZ6D1	126	14.3
WHEZ7D1	126	7.9
WHEEZD3	126	8.7
WHEEZD5	126	6.3
WHEEZD6	126	2.4
WHEEZD7	126	22.2
BRETHE2	126	40.5
BRETHE3	126	15.9
BRETHE4	126	7.9
BRETHE5	126	7.1

Variable	n	Prevalence (%)
BRETHE6	126	1.6
CHESTF1	126	75.4
CHESTF2	126	15.9
CHESTF3	126	11.9
HISTG1	126	9.5
G2HIST1A	126	16.7
G2HIST1B	126	14.3
G2HIST2A	126	21.4
G2HIST2B	126	20.6
G2HIST3A	126	14.3
G2HIST3B	126	4.0
G2HIST4A	126	19.0
G2HIST4B	126	7.1
G2HIST5A	126	7.9
G2HIST5B	126	7.9
G2HIST5E	126	0.8
G2HIST5F	126	0
HISTG3A	126	2.4
HISTG3AM	126	0
HISTG3B	126	0
HISTG3C	126	0.8
HISTG3E	3	0
HISTG3G1	3	0
HISTG3G2	3	0
HISTG3G3	3	0
HISTG3G4	3	66.7
HISTG3G5	3	0
HISTG3GN	3	66.7
HISTG4A	126	12.7
HISTG4B	126	0.8
HISTG4C	126	15.1
HISTG4D	126	59.5

Other variables:

Variable	n	Prevalence (%)
EXPA0	126	60.3
EXPB0	126	60.3
EXPPA0	126	54.0
EXPPB0	126	54.0
EXPS	126	38.1
EXPP	126	32.5
NICCAT	125	84.8
ETHCAT	126	92.9
TRACE3	90	73.3
TRACE4	90	44.4
TRACE5	90	32.2

APPENDIX 5.2 Significant Bivariate associations

(Level of significance = 5%;)

Significant outcome realtionships

X - Square results

OUTCOME	VARIABLES ASSOCIATED (direction of association)
TRACE3	EXPS (+)[a]; EXPP (-)
TRACE4	EXPP (+)[a]; NICCAT (-);
TRACE5	EXPA700 (+)[a]; NICCAT (-)
COUGHA1	NICCAT (+)[c];
COUGHA2	NICCAT (+)[c];
COUGHA3	NICCAT (+)[c];
COUGHA4	NICCAT (+)[c];
PHLEGMB2	EXPA0 (+)[b]; EXPA50 (+)[b]
PHLEGMB4	EXPPA0[c] (+);
EPSDEC1	EXPA100 (+)[b]; EXPPA100 (+)[b]; EXPPA250 (+)[b];
EPSDEC3	EXPPA250 (+)[b];
WHEZ1D1	NICCAT (+);
WHEZ5D1	EXPA0 (-)
WHEZ6D1	EXPA0 (-); EXPPA0 (-); EXPA50 (-)
WHEEZD3	EXPP (+);
WHEEZD5	EXPA700 (+)[b]; EXPPA700 (+)[b]
CHESTF2	NICCAT (-);
CHESTF3	NICCAT (-);
HISTG1	EXPA0 (+) ; EXPS (+); EXPP (+);
G2HIST1B	EXPA0 (-)
HISTG3A	NICCAT (-);
HISTG4A	EXPA100 (+)
HISTG4C	EXPA700 (+)
HISTG4D	EXPS (-); EXPP (-)

T-tests and Wilcoxons

TRACE3	SPARACE(+)a; SHERBACE (+)[a]
DIFFSAT	EXPA700 (+)[a]; EXPPA700 (+)[a];
DLCOUN	EXPPA0 (+);
FEFMAX	EXPA700 (+); EXPPA700 (+);
FEFMAX2	EXPPA700 (+)

Spearman and Pearson correlations

FEV1L	AGE (-)[d]; HEIGHTCM (+)[d]; WEIGHTKG (+)[d]; NICX (-)
FVCL	AGE (-)[d]; HEIGHTCM (+)[d]; WEIGHTKG (+)[d]
FEV1FVC	AGE (-)[d]
FEFMAX	HEIGHTCM (+)[d]; WEIGHTKG (+)[d]
FEFMAX2	WEIGHTKG (+)[d]
DLCOUN	AGE (-)[d]; HEIGHTCM (+)[d]; WEIGHTKG (+)[d]; NICX (-)
DLCOUN2	AGE (-)[d]; WEIGHTKG (-)[d]
ALV	HEIGHTCM (+)[d]; WEIGHTKG (+)[d]
DLVAMLM	SPARACE AGE (-)[d]

Other significant associations

T-tests and Wilcoxons

ALC	EXPPA250 (+)[f]; EXPPA700 (+)[f];
AGE	EXPPA700 (+)[e]

Spearman and Pearson correlations

AGE	DIFFHR (-)
HEIGHTCM	PERWLPRE (-)
WEIGHTKG	PERWLPRE (-)
NICX	DIFFHR (-)

+ : positive association
- : negative association

Important associations

"a" = Significant associations between exposure and exercise desaturation
"b" = Significant associations between long-term exposure and reported health
"c" = Significant associations between smoking and reported respiratory health
"d" = Significant associations between lung function and age, weight, height
"e" = Significant associations between long-term exposure and age
"f" = Significant associations between long-term exposure and alcohol consumption

Appendix 5.3 Summary of linear regression analysis of the effect of total long-term accumulated paraquat exposure on radiology

Table 1. Full model

Outcome : Profusion score

Predictor	Beta	SE(beta)	P-value	Partial R^2
AGE	0.008878	0.00657987	0.1799	0.0251
WEIGHTKG	-0.007780	0.00802597	0.3344	0.0043
HEIGHTCM	0.007304	0.01013215	0.4724	0.0050
NICX	0.004219	0.00419708	0.3169	0.0068
ALC	0.000008267	0.00001558	0.5966	0.0023
PARACE	-0.000099267	0.00009079	0.2765	0.0092

Model R^2 : 0.0527

Appendix 5.4 Summary of logistic regression analysis of the effect of long-term total cumulative paraquat exposure on reported respiratory symptoms

Table 1. Full models describing the relationship between long-term accumulated paraquat and reported respiratory symptoms

Outcome COUGHA1

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0311	0.0263	0.2370	1.032 (0.980-1.086)
HEIGHTCM	-0.00208	0.0350	0.9527	0.998 (0.932-1.069)
WEIGHTKG	-0.0501	0.0282	0.0763	0.951 (0.900-1.005)
NICX	-0.00730	0.0143	0.6101	0.993 (0.965-1.021)
ALC	0.000071	0.000061	0.2469	1.000 (1.000-1.000)
SCHOOL	0.00927	0.0627	0.8826	1.009 (0.893-1.141)
PARACE	-0.00051	0.000361	0 .1550	0.999 (0.999-1.000)

N = 124

Outcome COUGHA2

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.00658	0.0263	0.8025	0.993 (0.944-1.046)
HEIGHTCM	-0.0271	0.0359	0.4512	0.973 (0.907-1.044)
WEIGHTKG	-0.0531	0.0306	0.0824	0.948 (0.893-1.007)
NICX	0.00573	0.0145	0.6919	1.006 (0.978-1.035)
ALC	0.00009	0.000057	0.1163	1.000 (1.000-1.000)
SCHOOL	-0.0116	0.0639	0.8561	0.988 (0.872-1.120)
PARACE	-0.00031	0.000372	0.4106	1.000 (0.999-1.000)

N = 124

Outcome COUGHA3

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0363	0.0256	0.1565	1.037 (0.986-1.090)
HEIGHTCM	-0.00082	0.0347	0.9811	0.999 (0.933-1.069)
WEIGHTKG	-0.0465	0.0286	0.1043	0.955 (0.902-1.010)
NICX	-0.00082	0.0143	0.9541	0.999 (0.972-1.028)
ALC	0.000027	0.000055	0.6190	1.000 (1.000-1.000)
SCHOOL	-0.0130	0.0625	0.8354	0.987 (0.873-1.116)
PARACE	-0.00054	0.000411	0.1899	0.999 (0.999-1.000)

N = 124

Outcome COUGHA4

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.00927	0.0273	0.7338	0.991 (0.939-1.045)
HEIGHTCM	0.0340	0.0375	0.3646	1.035 (0.961-1.113)
WEIGHTKG	-0.0859	0.0338	0.0111	0.918 (0.859-0.981)
NICX	0.00229	0.0153	0.8806	1.002 (0.973-1.033)
ALC	0.000125	0.000061	0.0419	1.000 (1.000-1.000)
SCHOOL	-0.0425	0.0660	0.5197	0.958 (0.842-1.091)
PARACE	-0.00028	0.000394	0.4829	1.000 (0.999-1.000)

N = 124 *

Outcome COUGHA5

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.00645	0.0367	0.8604	1.006 (0.937-1.082)
HEIGHTCM	-0.0144	0.0547	0.7920	0.986 (0.885-1.097)
WEIGHTKG	-0.0117	0.0435	0.7887	0.988 (0.908-1.076)
NICX	-0.0350	0.0370	0.3446	0.966 (0.898-1.038)
ALC	0.000034	0.000077	0.6607	1.000 (1.000-1.000)
SCHOOL	-0.1077	0.0943	0.2534	0.898 (0.746-1.080)
PARACE	-0.00041	0.000711	0.5601	1.000 (0.998-1.001)

N = 124

Outcome COUGHA7

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0220	0.0430	0.6084	1.022 (0.940-1.112)
HEIGHTCM	0.0452	0.0686	0.5095	1.046 (0.915-1.197)
WEIGHTKG	-0.0211	0.0513	0.6804	0.979 (0.885-1.083)
NICX	-0.0609	0.0547	0.2661	0.941 (0.845-1.048)
ALC	0.00004	0.00009	0.6551	1.000 (1.000-1.000)
SCHOOL	-0.1023	0.1161	0.3785	0.903 (0.719-1.134)
PARACE	-0.00015	0.000609	0.8038	1.000 (0.999-1.001)

N=124

Outcome PHLEGMB1

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.00675	0.0274	0.8056	0.993 (0.941-1.048)
HEIGHTCM	0.0493	0.0369	0.1814	1.051 (0.977-1.129)
WEIGHTKG	-0.0360	0.0301	0.2328	0.965 (0.909-1.023)
NICX	-0.0145	0.0194	0.4568	0.986 (0.949-1.024)
ALC	-0.00001	0.000059	0.8156	1.000 (1.000-1.000)
SCHOOL	-0.00876	0.0662	0.8948	0.991 (0.871-1.129)
PARACE	-0.00025	0.000414	0.5443	1.000 (0.999-1.001)

N=124

Outcome PHLEGMB2

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0230	0.0362	0.5259	0.977 (0.910-1.049)
HEIGHTCM	0.0788	0.0463	0.0885	1.082 (0.988-1.185)
WEIGHTKG	-0.0784	0.0418	0.0605	0.925 (0.852-1.003)
NICX	0.0128	0.0212	0.5459	1.013 (0.972-1.056)
ALC	-0.00012	0.000101	0.2444	1.000 (1.000-1.000)
SCHOOL	0.00473	0.0839	0.9551	1.005 (0.852-1.184)
PARACE	-0.00021	0.000685	0.7598	1.000 (0.998-1.001)

N=124

Outcome PHLEGMB3

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.00315	0.0297	0.9157	1.003 (0.946-1.063)
HEIGHTCM	0.0207	0.0398	0.6030	1.021 (0.944-1.104)
WEIGHTKG	-0.0374	0.0335	0.2646	0.963 (0.902-1.029)
NICX	-0.0172	0.0223	0.4411	0.983 (0.941-1.027)
ALC	-4.05E-7	0.000062	0.9948	1.000 (1.000-1.000)
SCHOOL	-0.00325	0.0729	0.9644	0.997 (0.864-1.150)
PARACE	-0.00015	0.000405	0.7189	1.000 (0.999-1.001)

N=124

Outcome PHLEGMB4

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.00224	0.0324	0.9449	1.002 (0.941-1.068)
HEIGHTCM	0.0620	0.0454	0.1724	1.064 (0.973-1.163)
WEIGHTKG	-0.0498	0.0380	0.1894	0.951 (0.883-1.025)
NICX	-0.00785	0.0230	0.7329	0.992 (0.948-1.038)
ALC	-0.00002	0.00007	0.8174	1.000 (1.000-1.000)
SCHOOL	-0.0294	0.0803	0.7144	0.971 (0.830-1.137)
PARACE	0.000087	0.000382	0.8191	1.000 (0.999-1.001)

N=124

Outcome PHLEGMB5

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0146	0.0428	0.7319	1.015 (0.933-1.103)
HEIGHTCM	0.0215	0.0561	0.7014	1.022 (0.915-1.141)
WEIGHTKG	-0.0214	0.0457	0.6387	0.979 (0.895-1.070)
NICX	-0.00245	0.0248	0.9212	0.998 (0.950-1.047)
ALC	4.079E-6	0.000082	0.9606	1.000 (1.000-1.000)
SCHOOL	0.0643	0.1069	0.5472	1.066 (0.865-1.315)
PARACE	0.000223	0.000388	0.5645	1.000 (0.999-1.001)

N=124

Outcome PHLEGMB7

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0114	0.0472	0.8099	0.989 (0.901-1.084)
HEIGHTCM	0.0911	0.0701	0.1935	1.095 (0.955-1.257)
WEIGHTKG	-0.0133	0.0518	0.7969	0.987 (0.892-1.092)
NICX	0.0158	0.0243	0.5153	1.016 (0.969-1.066)
ALC	-0.00009	0.000125	0.4883	1.000 (1.000-1.000)
SCHOOL	-0.0563	0.1137	0.6202	0.945 (0.756-1.181)
PARACE	0.000354	0.000492	0.4716	1.000 (0.999-1.001)

N=124

Outcome EPDSDEC1

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0309	0.0322	0.3368	1.031 (0.968-1.099)
HEIGHTCM	0.0372	0.0425	0.3804	1.038 (0.955-1.128)
WEIGHTKG	-0.0304	0.0340	0.3717	0.970 (0.907-1.037)
NICX	-0.0621	0.0334	0.0625	0.940 (0.880-1.003)
ALC	0.000074	0.00006	0.2203	1.000 (1.000-1.000)
SCHOOL	0.0687	0.0806	0.3941	1.071 (0.915-1.254)
PARACE	0.000384	0.000361	0.2870	1.000 (1.000-1.001)

N=124

Outcome EPSDEC3

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0291	0.0328	0.3746	1.030 (0.965-1.098)
HEIGHTCM	0.0556	0.0454	0.2211	1.057 (0.967-1.156)
WEIGHTKG	-0.0582	0.0380	0.1254	0.943 (0.876-1.016)
NICX	-0.0483	0.0327	0.1395	0.953 (0.894-1.016)
ALC	0.000071	0.000061	0.2448	1.000 (1.000-1.000)
SCHOOL	0.0165	0.0827	0.8424	1.017 (0.864-1.195)
PARACE	0.000417	0.000355	0.2410	1.000 (1.000-1.001)

N=124

Outcome WHEZD1

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0274	0.0265	0.3011	0.973 (0.924-1.025)
HEIGHTCM	0.0305	0.0357	0.3930	1.031 (0.961-1.106)
WEIGHTKG	-0.0621	0.0305	0.0415	0.940 (0.885-0.998)
NICX	0.00650	0.0145	0.6545	1.007 (0.978-1.036)
ALC	0.000111	0.000059	0.0592	1.000 (1.000-1.000)
SCHOOL	-0.0288	0.0628	0.6465	0.972 (0.859-1.099)
PARACE	-0.00007	0.000331	0.8293	1.000 (0.999-1.001)

N=124

Outcome WHEZ1D1

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0285	0.0265	0.2823	0.972 (0.923-1.024)
HEIGHTCM	0.0362	0.0358	0.3127	1.037 (0.967-1.112)
WEIGHTKG	-0.0643	0.0309	0.0375	0.938 (0.883-0.996)
NICX	0.0128	0.0145	0.3744	1.013 (0.985-1.042)
ALC	0.000067	0.000054	0.2161	1.000 (1.000-1.000)
SCHOOL	-0.0223	0.0626	0.7220	0.978 (0.865-1.106)
PARACE	0.000049	0.000315	0.8776	1.000 (0.999-1.001)

N=124

Outcome WHEZ2D1

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0360	0.0452	0.4254	0.965 (0.883-1.054)
HEIGHTCM	0.1173	0.0519	0.0237	1.124 (1.016-1.245)
WEIGHTKG	-0.1003	0.0469	0.0324	0.905 (0.825-0.992)
NICX	0.0311	0.0206	0.1309	1.032 (0.991-1.074)
ALC	-0.00011	0.00011	0.3048	1.000 (1.000-1.000)
SCHOOL	0.1112	0.1011	0.2711	1.118 (0.917-1.362)
PARACE	0.000306	0.000483	0.5259	1.000 (0.999-1.001)

N=124

Outcome WHEZ3D1

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0412	0.0343	0.2303	0.960 (0.897-1.026)
HEIGHTCM	-0.00297	0.0426	0.9443	0.997 (0.917-1.084)
WEIGHTKG	-0.0458	0.0387	0.2363	0.955 (0.885-1.030)
NICX	0.000076	0.0189	0.9968	1.000 (0.964-1.038)
ALC	0.000092	0.000062	0.1353	1.000 (1.000-1.000)
SCHOOL	-0.0281	0.0759	0.7110	0.972 (0.838-1.128)
PARACE	-0.00016	0.000452	0.7301	1.000 (0.999-1.001)

N=124

Outcome WHEZ4D1

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.00067	0.0302	0.9822	0.999 (0.942-1.060)
HEIGHTCM	0.0323	0.0394	0.4121	1.033 (0.956-1.116)
WEIGHTKG	-0.0408	0.0335	0.2241	0.960 (0.899-1.025)
NICX	0.0187	0.0150	0.2108	1.019 (0.989-1.049)
ALC	0.000103	0.000061	0.0910	1.000 (1.000-1.000)
SCHOOL	0.0704	0.0723	0.3302	1.073 (0.931-1.236)
PARACE	-0.00041	0.000474	0.3836	1.000 (0.999-1.001)

N=124

Outcome WHEZ5D1

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0304	0.0416	0.4646	0.970 (0.894-1.052)
HEIGHTCM	0.1037	0.0506	0.0406	1.109 (1.004-1.225)
WEIGHTKG	-0.0765	0.0446	0.0865	0.926 (0.849-1.011)
NICX	0.0190	0.0203	0.3499	1.019 (0.979-1.060)
ALC	-0.00001	0.000086	0.9031	1.000 (1.000-1.000)
SCHOOL	0.0451	0.0927	0.6266	1.046 (0.872-1.255)
PARACE	-0.00049	0.000807	0.5445	1.000 (0.998-1.001)

N=124

Outcome WHEZ6D1

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0364	0.0389	0.3498	1.037 (0.961-1.119)
HEIGHTCM	-0.0150	0.0504	0.7658	0.985 (0.893-1.087)
WEIGHTKG	-0.0846	0.0487	0.0821	0.919 (0.835-1.011)
NICX	-0.0154	0.0258	0.5504	0.985 (0.936-1.036)
ALC	0.00013	0.000066	0.0475	1.000 (1.000-1.000)
SCHOOL	0.0783	0.0995	0.4311	1.081 (0.890-1.314)
PARACE	-0.00022	0.000463	0.6361	1.000 (0.999-1.001)

N=124 *

Outcome WHEZ7D1

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0504	0.0544	0.3545	0.951 (0.855-1.058)
HEIGHTCM	0.1257	0.0682	0.0654	1.134 (0.992-1.296)
WEIGHTKG	-0.1303	0.0666	0.0505	0.878 (0.770-1.000)
NICX	-0.0207	0.0481	0.6667	0.980 (0.891-1.076)
ALC	0.000091	0.000093	0.3302	1.000 (1.000-1.000)
SCHOOL	-0.0906	0.1209	0.4537	0.913 (0.721-1.158)
PARACE	0.000331	0.00052	0.5238	1.000 (0.999-1.001)

N=124

Outcome WHEEZD3

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0169	0.0555	0.7605	0.983 (0.882-1.096)
HEIGHTCM	0.0334	0.0606	0.5817	1.034 (0.918-1.164)
WEIGHTKG	-0.0166	0.0497	0.7384	0.984 (0.892-1.084)
NICX	-0.0431	0.0486	0.3755	0.958 (0.871-1.054)
ALC	0.000059	0.000094	0.5264	1.000 (1.000-1.000)
SCHOOL	0.1413	0.1291	0.2736	1.152 (0.894-1.483)
PARACE	0.000406	0.000388	0.2949	1.000 (1.000-1.001)

N=124

Outcome WHEEZD6

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0461	0.0950	0.6273	1.047 (0.869-1.261)
HEIGHTCM	0.0405	0.1044	0.6980	1.041 (0.849-1.278)
WEIGHTKG	0.0300	0.0691	0.6638	1.030 (0.900-1.180)
NICX	-0.0559	0.0916	0.5417	0.946 (0.790-1.132)
ALC	-0.00013	0.000274	0.6341	1.000 (0.999-1.000)
SCHOOL	0.4247	0.3325	0.2015	1.529 (0.797-2.934)
PARACE	-0.00360	0.00540	0.5047	0.996 (0.986-1.007)

N=124

Outcome WHEEZD5

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0723	0.0718	0.3133	0.930 (0.808-1.071)
HEIGHTCM	0.1144	0.0774	0.1397	1.121 (0.963-1.305)
WEIGHTKG	-0.0592	0.0651	0.3633	0.943 (0.830-1.071)
NICX	-0.0113	0.0474	0.8110	0.989 (0.901-1.085)
ALC	0.000118	0.000103	0.2523	1.000 (1.000-1.000)
SCHOOL	0.0383	0.1453	0.7919	1.039 (0.782-1.381)
PARACE	0.000701	0.000451	0.1198	1.001 (1.000-1.002)

N=124

Outcome WHEEZD7

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0312	0.0320	0.3292	0.969 (0.910-1.032)
HEIGHTCM	0.0397	0.0426	0.3514	1.040 (0.957-1.131)
WEIGHTKG	-0.0541	0.0377	0.1511	0.947 (0.880-1.020)
NICX	0.00526	0.0178	0.7675	1.005 (0.971-1.041)
ALC	0.000045	0.000061	0.4662	1.000 (1.000-1.000)
SCHOOL	-0.0675	0.0742	0.3632	0.935 (0.808-1.081)
PARACE	0.000071	0.000379	0.8516	1.000 (0.999-1.001)

Outcome BRETHE2

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.00682	0.0289	0.8136	1.007 (0.951-1.066)
HEIGHTCM	0.1148	0.0423	0.0067	1.122 (1.032-1.219)
WEIGHTKG	-0.1404	0.0392	0.0003	0.869 (0.805-0.938)
NICX	0.00174	0.0159	0.9133	1.002 (0.971-1.034)
ALC	0.000157	0.000068	0.0217	1.000 (1.000-1.000)
SCHOOL	-0.0129	0.0692	0.8524	0.987 (0.862-1.131)
PARACE	-0.00036	0.000449	0.4165	1.000 (0.999-1.001)

N=124 *

Outcome BRETHE3

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0127	0.0334	0.7037	1.013 (0.949-1.081)
HEIGHTCM	0.0777	0.0510	0.1274	1.081 (0.978-1.194)
WEIGHTKG	-0.0766	0.0438	0.0805	0.926 (0.850-1.009)
NICX	0.00965	0.0178	0.5883	1.010 (0.975-1.046)
ALC	0.000122	0.000067	0.0688	1.000 (1.000-1.000)
SCHOOL	-0.0678	0.0848	0.4235	0.934 (0.791-1.103)
PARACE	-0.00036	0.000542	0.5050	1.000 (0.999-1.001)

N=124

Outcome BRETHE4

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0515	0.0527	0.3280	0.950 (0.857-1.053)
HEIGHTCM	0.000356	0.0716	0.9960	1.000 (0.869-1.151)
WEIGHTKG	-0.0162	0.0606	0.7886	0.984 (0.874-1.108)
NICX	-0.0336	0.0503	0.5037	0.967 (0.876-1.067)
ALC	0.000259	0.000092	0.0046	1.000 (1.000-1.000)
SCHOOL	-0.1632	0.1168	0.1623	0.849 (0.676-1.068)
PARACE	-0.00386	0.00323	0.2318	0.996 (0.990-1.002)

N=124 *

Outcome BRETHE5

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0320	0.0550	0.5605	1.033 (0.927-1.150)
HEIGHTCM	-0.0557	0.0723	0.4405	0.946 (0.821-1.090)
WEIGHTKG	-0.1096	0.0756	0.1470	0.896 (0.773-1.039)
NICX	0.0217	0.0233	0.3506	1.022 (0.976-1.070)
ALC	0.000148	0.000083	0.0731	1.000 (1.000-1.000)
SCHOOL	0.1457	0.1412	0.3020	1.157 (0.877-1.526)
PARACE	-0.00087	0.00106	0.4146	0.999 (0.997-1.001)

N=124

Outcome BRETHE6

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0231	0.0305	0.4483	1.023 (0.964-1.086)
HEIGHTCM	-0.0475	0.0399	0.2342	0.954 (0.882-1.031)
WEIGHTKG	0.0227	0.0326	0.4866	1.023 (0.960-1.091)
NICX	-0.0304	0.0162	0.0607	0.970 (0.940-1.001)
ALC	0.000111	0.000082	0.1778	1.000 (1.000-1.000)
SCHOOL	-0.00925	0.0722	0.8982	0.991 (0.860-1.142)
PARACE	0.000805	0.000825	0.3293	1.001 (0.999-1.002)

N=124

Outcome CHESTF2

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.00999	0.0378	0.7915	0.990 (0.919-1.066)
HEIGHTCM	0.0179	0.0476	0.7064	1.018 (0.927-1.118)
WEIGHTKG	0.0465	0.0355	0.1901	1.048 (0.977-1.123)
NICX	0.0218	0.0165	0.1859	1.022 (0.990-1.056)
ALC	-0.00005	0.000085	0.5727	1.000 (1.000-1.000)
SCHOOL	0.1022	0.0899	0.2554	1.108 (0.929-1.321)
PARACE	0.000075	0.000448	0.8671	1.000 (0.999-1.001)

N=124

Outcome CHESTF3

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0431	0.0475	0.3649	0.958 (0.873-1.051)
HEIGHTCM	-0.0188	0.0551	0.7326	0.981 (0.881-1.093)
WEIGHTKG	0.0720	0.0417	0.0843	1.075 (0.990-1.166)
NICX	0.0319	0.0184	0.0834	1.032 (0.996-1.070)
ALC	-0.00006	0.000112	0.5964	1.000 (1.000-1.000)
SCHOOL	0.0802	0.1034	0.4380	1.084 (0.885-1.327)
PARACE	-0.00009	0.000693	0.8976	1.000 (0.999-1.001)

N=124

Outcome HISTG1

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0874	0.0507	0.0845	0.916 (0.830-1.012)
HEIGHTCM	0.0156	0.0669	0.8150	1.016 (0.891-1.158)
WEIGHTKG	-0.0570	0.0645	0.3768	0.945 (0.832-1.072)
NICX	-0.0127	0.0456	0.7814	0.987 (0.903-1.080)
ALC	-0.00013	0.000149	0.3764	1.000 (1.000-1.000)
SCHOOL	-0.3193	0.1131	0.0047	0.727 (0.582-0.907)
PARACE	0.000313	0.000659	0.6343	1.000 (0.999-1.002)

N=124

Outcome G2HIST1A

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.00720	0.0314	0.8188	0.993 (0.934-1.056)
HEIGHTCM	-0.00316	0.0470	0.9464	0.997 (0.909-1.093)
WEIGHTKG	-0.0134	0.0374	0.7198	0.987 (0.917-1.062)
NICX	-0.0176	0.0247	0.4761	0.983 (0.936-1.031)
ALC	0.000015	0.000067	0.8176	1.000 (1.000-1.000)
SCHOOL	-0.1461	0.0803	0.0690	0.864 (0.738-1.011)
PARACE	0.000015	0.000399	0.9693	1.000 (0.999-1.001)

N=124

Outcome G2HIST1B

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0112	0.0329	0.7325	0.989 (0.927-1.055)
HEIGHTCM	0.0292	0.0521	0.5750	1.030 (0.930-1.140)
WEIGHTKG	-0.0368	0.0426	0.3875	0.964 (0.887-1.048)
NICX	-0.00940	0.0246	0.7019	0.991 (0.944-1.039)
ALC	0.000011	0.000072	0.8782	1.000 (1.000-1.000)
SCHOOL	-0.1993	0.0872	0.0222	0.819 (0.691-0.972)
PARACE	8.508E-6	0.000463	0.9853	1.000 (0.999-1.001)

N=124

Outcome G2HIST2A

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.00550	0.0294	0.8519	0.995 (0.939-1.054)
HEIGHTCM	0.0587	0.0435	0.1768	1.060 (0.974-1.155)
WEIGHTKG	-0.0292	0.0344	0.3962	0.971 (0.908-1.039)
NICX	0.00520	0.0195	0.7896	1.005 (0.968-1.044)
ALC	-0.00005	0.000071	0.5138	1.000 (1.000-1.000)
SCHOOL	-0.1384	0.0754	0.0665	0.871 (0.751-1.009)
PARACE	-0.00188	0.00126	0.1343	0.998 (0.996-1.001)

N=124

Outcome G2HIST2B

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.00365	0.0297	0.9023	0.996 (0.940-1.056)
HEIGHTCM	0.0536	0.0438	0.2215	1.055 (0.968-1.150)
WEIGHTKG	-0.0277	0.0347	0.4249	0.973 (0.909-1.041)
NICX	0.00246	0.0203	0.9035	1.002 (0.963-1.043)
ALC	-0.00004	0.000071	0.5735	1.000 (1.000-1.000)
SCHOOL	-0.1321	0.0761	0.0826	0.876 (0.755-1.017)
PARACE	-0.00192	0.00130	0.1389	0.998 (0.996-1.001)

N=124

Outcome G2HIST3A

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0716	0.0383	0.0616	1.074 (0.997-1.158)
HEIGHTCM	-0.0275	0.0501	0.5836	0.973 (0.882-1.073)
WEIGHTKG	-0.0333	0.0412	0.4190	0.967 (0.892-1.049)
NICX	-0.1452	0.0578	0.0120	0.865 (0.772-0.969)
ALC	0.000022	0.000076	0.7720	1.000 (1.000-1.000)
SCHOOL	0.0833	0.0999	0.4045	1.087 (0.894-1.322)
PARACE	-0.00004	0.000357	0.9014	1.000 (0.999-1.001)

N=124 *

Outcome G2HIST3B

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0118	0.0915	0.8976	1.012 (0.846-1.211)
HEIGHTCM	0.0901	0.1007	0.3713	1.094 (0.898-1.333)
WEIGHTKG	-0.00133	0.0718	0.9853	0.999 (0.868-1.150)
NICX	-0.2352	0.1305	0.0715	0.790 (0.612-1.021)
ALC	0.000352	0.000181	0.0517	1.000 (1.000-1.001)
SCHOOL	0.6107	0.3372	0.0701	1.842 (0.951-3.566)
PARACE	-0.00218	0.00157	0.1635	0.998 (0.995-1.001)

N=124

Outcome G2HIST4A

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.00091	0.0316	0.9772	0.999 (0.939-1.063)
HEIGHTCM	0.0159	0.0416	0.7030	1.016 (0.936-1.102)
WEIGHTKG	-0.00534	0.0335	0.8735	0.995 (0.931-1.062)
NICX	0.00579	0.0173	0.7383	1.006 (0.972-1.041)
ALC	0.000024	0.000063	0.7056	1.000 (1.000-1.000)
SCHOOL	0.0294	0.0774	0.7037	1.030 (0.885-1.199)
PARACE	-0.00149	0.00108	0.1655	0.999 (0.996-1.001)

N=124

Outcome G2HIST4B

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.000122	0.0492	0.9980	1.000 (0.908-1.101)
HEIGHTCM	0.0631	0.0680	0.3533	1.065 (0.932-1.217)
WEIGHTKG	0.0344	0.0460	0.4542	1.035 (0.946-1.133)
NICX	-0.00536	0.0287	0.8517	0.995 (0.940-1.052)
ALC	0.000084	0.000083	0.3120	1.000 (1.000-1.000)
SCHOOL	0.0198	0.1178	0.8664	1.020 (0.810-1.285)
PARACE	-0.00072	0.000993	0.4702	0.999 (0.997-1.001)

N=124

Outcome G2HIST5A

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0482	0.0461	0.2958	0.953 (0.871-1.043)
HEIGHTCM	0.0878	0.0802	0.2733	1.092 (0.933-1.278)
WEIGHTKG	-0.0791	0.0701	0.2590	0.924 (0.805-1.060)
NICX	0.0366	0.0291	0.2077	1.037 (0.980-1.098)
ALC	0.000089	0.000083	0.2842	1.000 (1.000-1.000)
SCHOOL	-0.3288	0.1235	0.0078	0.720 (0.565-0.917)
PARACE	-0.00519	0.00362	0.1513	0.995 (0.998-1.002)

N=124 *

Outcome G2HIST5B

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0482	0.0461	0.2958	0.953 (0.871-1.043)
HEIGHTCM	0.0878	0.0802	0.2733	1.092 (0.933-1.278)
WEIGHTKG	-0.0791	0.0701	0.2590	0.924 (0.805-1.060)
NICX	0.0366	0.0291	0.2077	1.037 (0.980-1.098)
ALC	0.000089	0.000083	0.2842	1.000 (1.000-1.000)
SCHOOL	-0.3288	0.1235	0.0078	0.720 (0.565-0.917)
PARACE	-0.00519	0.00362	0.1513	0.995 (0.988-1.002)

N=124 *

Outcome G2HIST5E

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.1095	0.0970	0.2588	1.116 (0.923-1.349)
HEIGHTCM	-0.0629	0.1280	0.6231	0.939 (0.731-1.207)
WEIGHTKG	-0.2293	0.1521	0.1317	0.795 (0.590-1.071)
NICX	-0.0398	0.0773	0.6066	0.961 (0.826-1.118)
ALC	-0.00008	0.000198	0.6849	1.000 (1.000-1.000)
SCHOOL	0.0311	0.2405	0.8970	1.032 (0.644-1.653)
PARACE	-0.00320	0.00465	0.4906	0,997 (0.988-1.006)

N=124

Outcome HISTG3C

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0468	0.0413	0.2573	1.048 (0.966-1.136)
HEIGHTCM	-0.0628	0.0498	0.2071	0.939 (0.852-1.035)
WEIGHTKG	0.0226	0.0391	0.5635	1.023 (0.947-1.104)
NICX	-0.0128	0.0224	0.5682	0.987 (0.945-1.032)
ALC	0.000016	0.000078	0.8417	1.000 (1.000-1.000)
SCHOOL	0.2263	0.1111	0.0417	1.254 (1.009-1.559)
PARACE	-0.00044	0.00064	0.4914	1.000 (0.998-1.001)

N=124

Outcome HISTG4B

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.0484	0.0398	0.2241	0.953 (0.881-1.030)
HEIGHTCM	0.0137	0.0507	0.7875	1.014 (0.918-1.120)
WEIGHTKG	-0.00134	0.0413	0.9742	0.999 (0.921-1.083)
NICX	0.0118	0.0175	0.4983	1.012 (0.978-1.047)
ALC	0.000124	0.000066	0.0581	1.000 (1.000-1.000)
SCHOOL	-0.0672	0.0842	0.4249	0.935 (0.793-1.103)
PARACE	0.000374	0.000341	0.2717	1.000 (1.000-1.001)

N=124

Outcome HISTG4D

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	-0.00226	0.0250	0.9278	0.998 (0.950-1.048)
HEIGHTCM	-0.0270	0.0343	0.4313	0.973 (0.910-1.041)
WEIGHTKG	0.0189	0.0273	0.4879	1.019 (0.966-1.075)
NICX	-0.00907	0.0139	0.5147	0.991 (0.964-1.018)
ALC	0.000046	0.000054	0.4007	1.000 (1.000-1.000)
SCHOOL	0.00641	0.0612	0.9166	1.006 (0.893-1.135)
PARACE	-0.00013	0.000304	0.6724	1.000 (0.999-1.000)

* Model p-value < 0.05

Appendix 5.5 Summary of linear regression analysis of the effect of total long-term cumulative paraquat exposure on respiratory function

Table1 Models describing the relationship between long-term accumulated paraquat exposure and respiratory function

Outcome: FEV1L, full model

Predictor	Beta	SE(beta)	Stand. Beta	P-value	Partial R^2
AGE	-0.030557	0.00488539	-0.53800672	0.0001	0.2506
HEIGHTCM	0.016363	0.00752287	0.19709139	0.0316	0.0389
WEIGHTKG	0.018390	0.00595908	0.28893941	0.0025	0.0753
NICX	-0.002029	0.00311623	-0.05093601	0.5163	0.0036
ALC	0.000012840	0.00001156	0.09150987	0.2692	0.0104
PARACE	0.000046939	0.00006741	0.05202026	0.4876	0.0041

Model R-square 0.3922 *

Outcome: FVCL, full model

Predictor	Beta	SE(beta)	Stand. Beta	P-value	Partial R^2
AGE	-0.019442	0.00528658	-0.32055642	0.0004	0.1036
HEIGHTCM	0.037939	0.00814065	0.42794012	0.0001	0.1566
WEIGHTKG	0.009432	0.00644844	0.13877921	0.1462	0.0180
NICX	-0.003208	0.00337213	-0.07542408	0.3434	0.0077
ALC	0.000002831	0.00001251	0.01889198	0.8214	0.0004
PARACE	-0.000022848	0.00007295	-0.02371271	0.7547	0.0008

Model R-square 0.3758 *

Outcome: DLCOUN, full model

Predictor	Beta	SE(beta)	Stand. Beta	P-value	Partial R^2
AGE	-0.041524	0.0076933	-0.54965180	0.0001	0.2273
HEIGHTCM	0.018571	0.0110218	0.17236190	0.0952	0.0279
WEIGHTKG	0.025018	0.0087698	0.30356085	0.0053	0.0760
NICX	-0.002910	0.0044119	-0.05737864	0.5113	0.0044
ALC	0.000037	0.0000169	0.20853946	0.0296	0.0469
PARACE	0.000074	0.0000940	0.06537023	0.4336	0.0062

Model R-square 0.3646 *

Outcome: DLVAMLM, full model

Predictor	Beta	SE(beta)	Stand. Beta	P-value	Partia R^2
AGE	-0.007456	0.0015586	-0.54506957	0.0001	0.187
HEIGHTCM	-0.002357	0.0022335	-0.12082394	0.2939	0.011
WEIGHTKG	0.001266	0.0017771	0.08481193	0.4781	0.005
NICX	0.000510	0.0008941	0.05555204	0.5698	0.003
ALC	0.000005510	0.0000034	0.17197642	0.1070	0.026
PARACE	0.000002412	0.0000191	0.01205595	0.8972	0.000

Model R-square 0.2041 *

Outcome: FEFMAX, full model

Predictor	Beta	SE(beta)	Stand. Beta	P-value	Partia R^2
AGE	-0.055908	0.01783648	-0.29387386	0.0022	0.077
HEIGHTCM	0.030962	0.02746588	0.11133838	0.2619	0.010
WEIGHTKG	0.087250	0.02175653	0.40926860	0.0001	0.120
NICX	-0.001584	0.01137731	-0.01187078	0.8895	0.000
ALC	0.000044104	0.00004222	0.09384480	0.2984	0.009
PARACE	0.000471	0.00024611	0.15585044	0.0581	0.030

Model R-square 0.2778 *

Outcome: FEFMAX, forward selection model

Predictor	Beta	SE(beta)	Stand. Beta	P-value	Partia R^2
AGE	-0.05234435	0.01550276	-0.27514392	0.0010	0.058
WEIGHTKG	0.09985086	0.01715390	0.46837796	0.0001	0.174
PARACE	0.00052384	0.00024058	0.17331976	0.0314	0.029

Model R-square 0.2612 *

* Model p-value < 0.05

Appendix 5.6 Summary of linear regression analysis of the effect of long-term total cumulative paraquat exposure on the maximum workload achieved in exercise testing (MAXWL).

Table1 Full model and model with lowest CIA criterion.

Outcome: MAXWL (full model)

Predictor	Beta	SE(beta)	Stand. Beta	P-value	Partial R^2
AGE	-5.943452	1.63491649	-0.34849142	0.0004	0.1307
WEIGHTKG	7.032828	1.85095246	0.38321098	0.0002	0.0810
HEIGHTCM	-4.194959	2.37415961	-0.17499029	0.0800	0.0079
NICX	-1.054923	0.95491531	-0.09266777	0.2716	0.0074
ALC	0.00002969	0.00003796	0.07001668	0.4358	0.0150
DIFFHR	3.474230	0.80871262	0.35066556	0.0001	0.1422
RESTSAT	-3.693665	6.82791875	-0.04280552	0.5896	0.0026
PARACE	-0.007571	0.02070686	-0.02933506	0.7153	0.0012

Model R^2: 0.3414

Outcome: MAXWL (forward selection model)

Predictor	Beta	SE(beta)	Stand. Beta	P-value	Partial R^2
AGE	-5.93201	1.39258	-0.34782035	0.0001	0.1858
WEIGHTKG	6.47271	1.78731	0.35269050	0.0004	0.0668
HEIGHTCM	-3.82188	2.29211	-0.15942765	0.0981	0.0617
DIFFHR	3.57833	0.78939	0.36117316	0.0001	0.0160

Model R^2: 0.3303

Appendix 5.7 Correlation matrix of variables in the model describing the relationship between total average lifetime paraquat exposure to exercise oxygen desaturation

VARIABLES	INTERCEP	AGE	WEIGHTKG	NICX
INTERCEP	1.0000	-0.4404	-0.4619	0.0507
AGE	-0.4404	1.0000	-0.2279	-0.1823
WEIGHTKG	-0.4619	-0.2279	1.0000	-0.1410
NICX	0.0507	-0.1823	-0.1410	1.0000
ALC	0.0996	-0.4194	0.0752	-0.0923
DIFFHR	-0.7570	0.3173	-0.1020	0.0681
PARINT	0.0215	0.1720	-0.0550	0.0011

VARIABLES	ALC	DIFFHR	PARINT
INTERCEP	0.0996	-0.7570	0.0215
AGE	-0.4194	0.3173	0.1720
WEIGHTKG	0.0752	-0.1020	-0.0550
NICX	-0.0923	0.0681	0.0011
ALC	1.0000	-0.0982	-0.3100
DIFFHR	-0.0982	1.0000	-0.1067
PARINT	-0.3100	-0.1067	1.0000

Appendix 5.8 Multivariate analysis of the effect of paraquat exposure o exercise oxygen desaturation.

Table 1 Multiple linear regression analysis of the relationship betwee paraquat exposure and exercise oxygen desaturation using a number o exposure variables.

a) Full models

b) Model selected by stepwise and C_p procedures (lowest C_p)

a) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand.ß	P-value	Partial R^2
AGE	0.026108	0.03021703	0.111	0.3901	0.0007
WEIGHTKG	-0.060853	0.02785492	-0.239	0.0318	0.0431
NICX	0.006971	0.01804779	0.043	0.7003	0.0012
ALC	-0.000001098	0.00000168	-0.085	0.5158	0.0026
DIFFHR	0.015721	0.01769700	0.100	0.3770	0.0140
PARACE	0.001141	0.00056445	0.243	0.0464	0.0474

Model R^2: 0.1055 (p=0.154)

b) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
WEIGHTKG	-0.052885	0.02622634	-0.20782560	0.0469	0.0431
PARACE	0.001067	0.00048382	0.22721595	0.0302	0.0464

Model R^2: 0.0894 (p=0.0178)

a) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
AGE	0.034968	0.03033325	0.148	0.2523	0.0007
WEIGHTKG	-0.062021	0.02760924	-0.243	0.0274	0.0431
NICX	0.006676	0.01787788	0.041	0.7098	0.0012
ALC	-0.000000674	0.00000155	-0.052	0.6656	0.0026
DIFFHR	0.014989	0.01753500	0.095	0.3951	0.0140
PARINT	0.019419	0.00811618	0.264	0.0190	0.0652

Model R^2: 0.122 (p=0.0902)

b) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2

WEIGHTKG	-0.051420	0.02601466	-0.20206899	0.0513	0.0408
PARINT	0.018563	0.00750381	0.25290945	0.0153	0.0611

Model R^2: 0.1019 (p=0.010)

a) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
AGE	0.031615	0.03115917	0.134	0.3133	0.0007
WEIGHTKG	-0.061969	0.02826237	-0.243	0.0312	0.0431
NICX	0.000701	0.01870944	0.004	0.9702	0.0012
ALC	-0.000000618	0.00000169	-0.047	0.7152	0.0026
DIFFHR	0.015958	0.01796931	0.101	0.3771	0.0140
SPARACE	0.011981	0.00825626	0.179	0.1506	0.0250

Model R-2 0.0844 (p=0.2851)

b) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial
WEIGHTKG	-0.053979	0.02661255	-0.212	0.0456	0.03795
SNDPT	0.011685	0.00696639	0.175	0.0971	0.03167

Model R-2 0.0685 (p=0.0412)

a) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
AGE	0.027814	0.03021759	0.118	0.3600	0.0007
WEIGHTKG	-0.059930	0.02778871	-0.235	0.0340	0.0431
NICX	0.006663	0.01801505	0.0412	0.7124	0.0012
ALC	-0.000001150	0.00000168	-0.089	0.4954	0.0026
DIFFHR	0.017798	0.01758673	0.113	0.3145	0.0140
HERBACE	0.001169	0.00055748	0.249	0.0391	0.0508

Model R^2: 0.1087 (p=0.1398)

b) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partia R^2
WEIGHTKG	-0.051693	0.02619007	-0.203	0.0516	0.0412
HERBACE	0.001071	0.00048211	0.228	0.0289	0.0490

Model R-2 0.0902 (p=0.0371)

a) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
AGE	0.036433	0.03044884	0.155	0.2349	0.0007
WEIGHTKG	-0.061118	0.02759370	-0.240	0.0295	0.0431
NICX	0.006415	0.01787975	0.039	0.7207	0.0012
ALC	-0.000000669	0.00000155	-0.051	0.6680	0.0026
DIFFHR	0.016655	0.01747620	0.106	0.3434	0.0140
HERBINT	0.019370	0.00810713	0.263	0.0192	0.0650

Model R-2 0.0123 (p=0.0907)

b) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
WEIGHTKG	-0.050234	0.02603662	-0.197	0.0570	0.0379
HERBINT	0.018300	0.00753406	0.249	0.0172	0.0642

Model R-2 0.0997 (p=0.0109)

a) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
AGE	0.025286	0.03022219	0.107	0.4052	0.0007
WEIGHTKG	-0.060548	0.02787290	-0.237	0.0327	0.0431
NICX	0.007551	0.01806819	0.046	0.6771	0.0012
ALC	-0.000001019	0.00000167	-0.079	0.5438	0.0026
DIFFHR	0.015996	0.01770109	0.102	0.3688	0.0140
PARACE2	0.001161	0.00058466	0.237	0.0504	0.0458

Model R^2 0.104 (P=0.1616)

b) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
WEIGHTKG	-0.052569	0.02623902	-0.206	0.0483	0.0426
PARACE2	0.001098	0.00050507	0.224	0.0325	0.0455

Model R^2: 0.0881 (p=0.019)

a) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
AGE	0.033884	0.03032109	0.144	0.2670	0.0007
WEIGHTKG	-0.062197	0.02765706	-0.244	0.0272	0.0431
NICX	0.007047	0.01790570	0.043	0.6949	0.0012
ALC	-0.000000635	0.00000155	-0.049	0.6841	0.0026
DIFFHR	0.015520	0.01754263	0.099	0.3789	0.0140
PARINT2	0.019840	0.00848977	0.257	0.0219	0.0624

Model R^2: 0.120 (p=0.099)

b) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
WEIGHTKG	-0.05170960	0.02605384	-0.203	0.0504	0.0412
PARINT2	0.01909271	0.00787878	0.248	0.0175	0.0582

Model R^2: 0.100 (p=0.011)

a) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value 2	Partial R^2
AGE	0.029191	0.03098453	0.124	0.3445	0.0007
WEIGHTKG	-0.061908	0.02806421	-0.243	0.0302	0.0431
NICX	0.004571	0.01876367	0.028	0.8082	0.0012
ALC	-0.000001299	0.00000174	-0.100	0.4569	0.0026
DIFFHR	0.014885	0.01785821	0.095	0.4070	0.0140
SPARACE	0.004750	0.00955987	0.071	0.6206	0.0250
PARACE	0.000972	0.00066124	0.207	0.1453	0.0260

Model R^2: 0.110 (p=0.215)

b) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
WEIGHTKG	-0.052885	0.02622634	-0.20782560	0.0469	0.0431
PARACE	0.001067	0.00048382	0.22721595	0.0302	0.0464

Model R^2: 0.0894 (p=0.0178)

a) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
AGE	0.036120	0.03077473	0.153	0.2440	0.0007
WEIGHTKG	-0.062564	0.02783154	-0.245	0.0273	0.0431
NICX	0.005342	0.01858607	0.033	0.7745	0.0012
ALC	-0.000000837	0.00000167	-0.065	0.6165	0.0026
DIFFHR	0.014524	0.01771053	0.092	0.4146	0.0140
SPARACE	0.002690	0.00950157	0.040	0.7778	0.0250
PARINT	0.018022	0.00953921	0.245	0.0624	0.0422

Model R^2: 0.123 (p=0.141)

b) Outcome: DIFFSAT

Predictor	ß	SE(ß)	Stand. ß	P-value	Partial R^2
WEIGHTKG	-0.051420	0.02601466	-0.20206899	0.0513	0.0408
PARINT	0.018563	0.00750381	0.25290945	0.0153	0.0611

Model R^2: 0.1019 (p=0.010)

Table 2 Multiple Logistic Regression analysis of the effects of paraqu exposure on exercise desaturation dichotomised at various cut-offs usi a number of exposure indices. (Full models)

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0377	0.0284	0.1840	1.038 (0.984 - 1.093)
WEIGHTKG	-0.0378	0.0281	0.1777	0.964 (0.916 - 1.016)
NICX	-0.0112	0.0205	0.5825	0.989 (0.950 - 1.029)
ALC	-0.0000017	0.0000016	0.2707	1.000 (1.000 - 1.000)
DIFFHR	0.00052	0.0170	0.9752	1.001 (0.970 - 1.028)
EXPINT13	0.7361	0.5469	0.1783	2.088 (0.715 - 6.098)

N = 90

Outcome TRACE5

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0436	0.0293	0.1364	1.045 (0.985 - 1.109)
WEIGHTKG	-0.0409	0.0289	0.1563	0.960 (0.910 - 1.020)
NICX	-0.0230	0.0233	0.3231	0.977 (0.934 - 1.023)
ALC	-0.0000032	0.0000017	0.0863	1.000 (1.000 - 1.000)
DIFFHR	-0.00868	0.0176	0.6254	0.991 (0.958 - 1.026)
EXPINT34	1.5305	0.6970	0.0282	4.621 (1.178 - 18.128)

N = 90

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0377	0.0284	0.1840	1.038 (0.982 - 1.098)
WEIGHTKG	-0.0378	0.0281	0.1777	0.963 (0.911 - 1.017)
NICX	-0.0112	0.0204	0.5825	0.989 (0.950 - 1.029)
ALC	-0.0000017	0.0000016	0.2707	1.000 (1.000 - 1.000)
DIFFHR	0.00053	0.0170	0.9752	1.001 (0.968 - 1.034)
EXPA250	0.9566	0.5832	0.1010	2.604 (0.830 - 8.197)

N = 90

Outcome TRACE5

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0437	0.0294	0.1365	1.045 (0.986 - 1.107)
WEIGHTKG	-0.0409	0.0289	0.1565	0.960 (0.907 - 1.016)
NICX	-0.0230	0.0233	0.3231	0.977 (0.934 - 1.023)
ALC	-0.0000031	0.0000018	0.0867	1.000 (1.000 - 1.000)
DIFFHR	-0.00858	0.0176	0.6254	0.991 (0.958 - 1.026)
EXPA700	2.5201	0.9497	0.0080	12.430 (1.932 - 79.954)

N = 90

Outcome TRACE5

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0470	0.0297	0.1135	1.048 (0.989 - 1.111)
WEIGHTKG	-0.0388	0.0285	0.1724	0.962 (0.910 - 1.017)
NICX	-0.0111	0.0227	0.6235	0.983 (0.946 - 1.034)
ALC	-0.0000035	0.0000019	0.0723	1.000 (1.000 - 1.000)
DIFFHR	0.000681	0.0173	0.9686	1.001 (0.967 - 1.035)
HERBACE	0.00155	0.000604	0.0105	1.002 (1.000 - 1.003)

N = 90

Outcome TRACE5

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0567	0.0300	0.0592	1.058 (0.998 - 1.122)
WEIGHTKG	-0.0393	0.0285	0.1682	0.961 (0.909 - 1.017)
NICX	-0.0118	0.0231	0.6105	0.988 (0.944 - 1.034)
ALC	-0.0000026	0.0000175	0.1319	1.000 (1.000 - 1.000)
DIFFHR	-0.00133	0.0175	0.9394	0.999 (0.965 - 1.034)
HERBINT	0.0260	0.0106	0.0137	1.026 (1.005 - 1.048)

N = 90

Outcome TRACE3

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0433	0.0293	0.1389	1.044 (0.986 - 1.106)
WEIGHTKG	-0.0394	0.0284	0.1647	0.982 (0.909 - 1.016)
NICX	-0.0106	0.0223	0.6352	0.989 (0.947 - 1.034)
ALC	-0.0000033	0.0000019	0.0872	1.000 (1.000 - 1.000)
DIFFHR	-0.00226	0.0174	0.8968	0.998 (0.964 - 1.032)
PARACE	0.00143	0.000597	0.0166	1.001 (1.000 - 1.003)

N = 90

Outcome TRACE4

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0487	0.0295	0.0989	1.050 (0.991 - 1.112)
WEIGHTKG	-0.0401	0.0282	0.1543	0.961 (0.909 - 1.015)
NICX	-0.0185	0.0215	0.3886	0.982 (0.941 - 1.024)

ALC	-0.0000023	0.0000016	0.1684	1.000 (1.000 - 1.000)
DIFFHR	-0.00143	0.0170	0.9333	0.999 (0.966 - 1.033)
SPARACE	0.0142	0.00797	0.0743	1.014 (0.999 - 1.030)

N = 90

Outcome TRACE5

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0355	0.0290	0.2218	1.036 (0.979 - 1.097)
WEIGHTKG	-0.0405	0.0287	0.1586	0.960 (0.908 - 1.016)
NICX	-0.0147	0.0209	0.4837	0.985 (0.946 - 1.027)
ALC	-0.0000023	0.0000016	0.1765	1.000 (1.000 - 1.000)
DIFFHR	-0.00286	0.0172	0.8680	0.997 (0.964 - 1.031)
EXPPA516	1.6826	0.7445	0.0238	5.376 (1.250 - 23.256)

N = 90

Outcome TRACE3

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.0533	0.0297	0.0723	1.055 (0.995 - 1.118)
WEIGHTKG	-0.0401	0.0285	0.1594	0.961 (0.908 - 1.016)
NICX	-0.0114	0.0229	0.6193	0.989 (0.945 - 1.034)
ALC	-0.0000026	0.0000017	0.1404	1.000 (1.000 - 1.000)
DIFFHR	-0.00359	0.0177	0.8396	0.996 (0.962 - 1.032)
PARINT	0.0248	0.0103	0.0166	1.025 (1.005 - 1.046)

N = 90

Outcome TRACE4

AGE	-0.00103	0.0273	0.9700	0.999 (0.947 - 1.054)
WEIGHTKG	-0.0323	0.0263	0.2187	0.968 (0.920 - 1.019)
NICX	0.00828	0.0165	0.6170	1.008 (0.976 - 1.042)
ALC	-6.79×10^{-7}	1.43×10^{-6}	0.6354	1.000 (1.000 - 1.000)
DIFFHR	0.00963	0.0160	0.5475	1.010 (0.978 - 1.042)
EXPPA516	0.9993	0.6944	0.1501	2.717 (0.696 - 10.64)

N = 90

Outcome TRACE3

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.00505	0.0303	0.8676	1.005 (0.947 - 1.067)
WEIGHTKG	-0.0440	0.0290	0.1298	0.957 (0.904 - 1.013)
NICX	0.0254	0.0274	0.3536	1.026 (0.972 - 1.082)
ALC	-0.0000027	0.0000022	0.1809	1.000 (1.000 - 1.000)
DIFFHR	0.0330	0.0188	0.0791	1.034 (0.996 - 1.072)

Outcome TRACE3

Predictor	Beta	SE(beta)	P-value	Odds Ratio and 95% CI
AGE	0.00505	0.0303	0.8676	1.005 (0.947 - 1.067)
WEIGHTKG	-0.0440	0.0290	0.1298	0.957 (0.904 - 1.013)
NICX	0.0254	0.0274	0.3536	1.026 (0.972 - 1.082)
ALC	-0.0000027	0.0000022	0.1809	1.000 (1.000 - 1.000)
DIFFHR	0.0330	0.0188	0.0791	1.034 (0.996 - 1.072)
EXPPA516	1.2725	1.1322	0.2610	3.571 (0.388 - 3.333)

N = 90